# THE AMERICAN HEART JOURNAL

©Am. Ht. Assn.

A JOURNAL FOR THE STUDY OF THE CIRCULATION

PUBLISHED MONTHLY

UNDER THE EDITORIAL DIRECTION OF

THE AMERICAN HEART ASSOCIATION

Fred M. Smith - - - - - - Editor-in-Chief

Associate Editors

Hugh McCulloch

Irving S. Wright

Horace M. Korns

---

Editorial Board

EDGAR V. ALLEN
CLAUDE S. BECK
HARRY GOLDBLATT
GEORGE HERRMANN
WILLIAM J. KERR
ROBERT L. LEVY
H. M. MARVIN
JONATHAN C. MEAKINS
ROY W. SCOTT
ISAAC STARR
J. MURRAY STEELE
PAUL D. WHITE
FRANK N. WILSON
CHARLES C. WOLFERTH

---

VOLUME 15
JANUARY—JUNE, 1938

---

ST. LOUIS
THE C. V. MOSBY COMPANY
1938

COPYRIGHT, 1938, BY THE C. V. MOSBY COMPANY

*(All rights reserved)*

(Printed in U. S. A.)

*Press of*
*The C. V. Mosby Company*
*St. Louis*

JAN 26 1938

Vol. 15 JANUARY, 1938 No. 1

MEDICAL LIBRARY

# THE AMERICAN HEART JOURNAL

© Am. Ht. Assn.

A JOURNAL FOR THE STUDY OF THE CIRCULATION

PUBLISHED MONTHLY
UNDER THE EDITORIAL DIRECTION OF
THE AMERICAN HEART ASSOCIATION

FRED M. SMITH.....Editor-in-Chief

Associate Editors
HUGH McCULLOCH
IRVING S. WRIGHT
HORACE M. KORNS

EDITORIAL BOARD

EDGAR V. ALLEN
CLAUDE S. BECK
HARRY GOLDBLATT
GEORGE HERRMANN
WILLIAM J. KERR
ROBERT L. LEVY
H. M. MARVIN
JONATHAN C. MEAKINS
ROY W. SCOTT
ISAAC STARR
J. MURRAY STEELE
PAUL D. WHITE
FRANK N. WILSON
CHARLES C. WOLFERTH

PUBLISHED BY THE C. V. MOSBY COMPANY, 3525 PINE BLVD., ST. LOUIS, U. S. A.

Copyright 1938 by The C. V. Mosby Company

CONTENTS ON INSIDE COVER

# The American Heart Journal

## CONTENTS FOR JANUARY, 1938

### Original Communications


The Significance of Rheumatic Activity in Chronic Rheumatic Heart Disease. Part I. Intensity and Extent. Irving B. Juster, M.D., Glens Falls, N. Y. ---- 1

The Precipitating Causes of Congestive Heart Failure. William A. Sodeman, M.D., and George E. Burch, M.D., New Orleans, La. ---- 23

Relation of Myocardial Disease to Abnormalities of the Ventricular Complex of the Electrocardiogram. Harold E. B. Pardee, M.D., and Leo Price, M.D., New York, N. Y. ---- 28

Observations on the Cardio-Accelerator Reflex From Stimulation of the Skin Temperature Receptors. Simon Benson, Ph.D., Chicago, Ill. ---- 45

The Calcified Nodular Deformity of the Aortic Valve. B. J. Clawson, M.D., J. F. Noble, M.D., and N. H. Lufkin, M.D., Minneapolis, Minn. ---- 53

The Influence of the Size of Cardiac Infarcts Upon the Electrocardiogram. Harry Gold, M.D., Walter Modell, M.D., and Janet Travell, M.D., New York, N. Y. ---- 77

Respiratory Changes Produced in the Cardiac Patient by Rebreathing Experiments as Compared With Those of the Normal Individual. Harry Landt, M.D., and Julien E. Benjamin, M.D., Cincinnati, Ohio ---- 83

Electrocardiographic Changes Following the Inhalation of Tobacco Smoke. Ashton Graybiel, M.D., Boston, Mass., Robert S. Starr, M.D., Hartford, Conn., and Paul D. White, M.D., Boston, Mass. ---- 89

Electrical Alternans Occurring in a Case With Pericardial Effusion. L. Feldman, M.D., Chicago, Ill. ---- 100


### Special Article


Standardization of Precordial Leads. Joint Recommendations of the American Heart Association and the Cardiac Society of Great Britain and Ireland ---- 107


### Department of Clinical Reports


Brucella Melitensis Bacteremia Associated With Vegetative Endocarditis. Daniel F. Levy, M.D., New Haven, Conn., and Benjamin Singerman, M.D., Burlington, Vt. ---- 109

Paroxysmal Auricular Fibrillation in the Course of Right Heart Failure due to Chronic Pulmonary Tuberculosis. Milton B. Rosenblatt, M.D., New York, N. Y. ---- 114

Reversible Bundle-Branch Block in a Case of Toxic Goiter. Victor A. Digilio, M.D., Philadelphia, Pa. ---- 116

Hyperpyrexia as a Complication of Rheumatic Fever. John A. Boone, M.D., Charleston, S. C. ---- 119


### Editorial


Editorial ---- 123


### Department of Reviews and Abstracts


Selected Abstracts ---- 124



Vol. 15, No. 1, January, 1938. American Heart Journal is published monthly by The C. V. Mosby Company, 3523 Pine Blvd., St. Louis, Mo. Subscription Price: United States, its Possessions, Pan-American Countries, Canada, $8.50 a year; Foreign, $9.50. Entered as Second-Class Matter at Post Office at St. Louis, Mo., under Act of March 3, 1879.

medical
Wahr

The American Heart Journal

VOL. 15 JANUARY, 1938 NO. 1

## Original Communications

# THE SIGNIFICANCE OF RHEUMATIC ACTIVITY IN CHRONIC RHEUMATIC HEART DISEASE*

### PART I. INTENSITY AND EXTENT

IRVING R. JUSTER, M.D.
GLENS FALLS, N. Y.

DURING the past few years further study of rheumatic heart disease has resulted in more comprehensive knowledge of the clinical and pathological facts concerning it. The occurrence of cardiac injury incident to acute rheumatic polyarthritis, chorea, and tonsillitis is well known,[1-14] and efforts are now made early to prevent damage to the heart.[2, 8, 12, 13, 15-30]

There exist, nevertheless, many adult patients who are incapacitated from rheumatic cardiac disease. How to manage them is still relatively poorly understood. They offer a complex therapeutic and social problem for which a satisfactory solution has not yet been found.

Recent observers have regarded the late stages of rheumatic cardiac disease as the end-result of an infection long since subsided.[31-35] Studies of rheumatic lesions[2, 11, 14, 24, 36-50] substantiate the importance of the continuance of the active inflammatory process. Impairment of cardiac function cannot always be attributed, therefore, solely to mechanical strain on the myocardium from stenosed and insufficient valves.

The marked disability of older patients and many of the symptoms and signs exhibited by them resemble similar phenomena presented by

*This article is the second of a series to be published on investigations at the New York Cardiac Shop, which was a special project of the Committee on Cardiac Clinics of the New York Heart Association. This work was made possible by grants from the Hofheimer Foundation for three years, the New York Foundation for two years, and the Altman Foundation for one year. The remainder of the fund was raised by the Board of Directors of the New York Cardiac Shop. This board was created by the Board of Directors of Irvington House.

All follow-up data were obtained from the various cardiac clinics and hospitals in New York City through the efforts of Miss Claire Lingg of the New York Heart Association. In a few instances patients died and no data were obtainable. The diagnoses on death certificates were then utilized.

Thanks are due Doctor Alfred E. Cohn and Doctor Homer F. Swift for advice and criticism. I also wish to acknowledge my appreciation to the following individuals and organizations for their cooperation and interest during the investigation: Doctor Edward Holtz, Miss Dorothy Frank, Miss Katharine West; the Board of Directors of the Y. W. H. A., Mrs. Felix Warburg, chairman; the Board of Directors of Irvington House, Mrs. Louis Levy, chairman; the Board of Directors of the New York Cardiac Shop, Mrs. Jack Wildberg, chairman; and Burroughs Wellcome and Company.

rheumatic patients recently "recovered" from the disease. The cardiac disability in the younger group arises presumably from persistence of the active rheumatic process, and definite evidence of this has repeatedly been found.[51-54] Because of this experience this investigation was undertaken in order to learn whether active infection persists in older ambulant patients and, if so, what is its intensity and extent. With a view, furthermore, to aiding patients financially embarrassed, and to studying them under the conditions prevailing in a sheltered workshop, the New York Cardiac Shop was organized in November, 1928. The study continued until Jan. 25, 1932.

## SELECTION OF CASES

Patients were referred by the hospitals and cardiac clinics in New York. At first cases classified as IIB[55] were accepted. Later when the presence of rheumatic activity in most patients became evident those in all functional classes were admitted. The 59 patients studied ranged between fifteen and forty-four years of age. They were observed from one to thirty-nine months, the average being 13.7 months. Their lesions were of the mitral or aortic valves or a combination of both. Patients suffering from syphilis were excluded.

## METHODS

A history was obtained on admission. A physical examination was made at least once a week. The results were recorded on Charts 1, 2, and 3 of the New York Heart Association. The incidence and intensity of all symptoms were noted daily and recorded on a special chart. The rectal temperature was taken for five minutes and the pulse was counted for one minute daily at 10:00 A.M. and 2:00 P.M. Roentgen-ray photographs at 2-meters were taken in the anteroposterior and right anterooblique positions; and fluoroscopic examinations of the chest in the anteroposterior and both lateral positions were made on admission and when necessary thereafter. Electrocardiograms were taken fortnightly. The leucocytes were counted weekly, between the hours of 10:30 A.M. and 12:00 noon when possible, under the same conditions as described in a previous communication.[56]

## EVIDENCE OF CHRONICITY

The literature concerning the value of the temperature, pulse, and leucocyte counts as indices of activity presents many conflicting opinions.

*Leucocyte Count.*—Swift, Miller, and Boots[57] noticed that in the continuous type of rheumatic fever in which cardiac involvement is the salient feature the count drops occasionally to normal, as in their Case 4, preceding the last cycle of fever and tachycardia before recovery. They suggested that "counts must be made frequently enough and over a sufficient period of time to set forth the trend of the leucocyte curve." Patients with marked clinical evidence of carditis exhibited the most pro-

longed leucocytosis. Thayer[58] was of the opinion that fever and leucocytosis were clear indications of carditis. According to Bezançon and Weil,[59] in uncomplicated cases of carditis of moderate severity the count was generally from 13,000 to 16,000; in milder forms slight leucocytosis was present, and in cases not accompanied by inflammatory reaction there was no leucocytosis. Bedford[60] observed in affected children no counts below 10,000 in fatal cases. Wilson and Koppel[52] in a group ranging from four to fifteen years of age, with chronic rheumatic heart disease, frequently found leucocytosis without other evidence of infection. Findlay[61] thought leucocyte counts of no value, and stated that Coombs and Perry were of like opinion.

Ernstene,[62] in a study similar to that of Swift, Miller, and Boots,[57] concluded that the corrected sedimentation rate was a more sensitive procedure than the leucocyte count. Peterman and Seeger,[63] however, preferred leucocyte and differential counts particularly in showing the clinical course of the disease. Swift[11] regards both procedures as valuable indices.

Isolated counts are doubtless of little value, particularly in lower degrees of activity; only by making repeated counts over an extended period can the trend be properly estimated. The greater the activity the more persistent is leucocytosis. A difficulty in arriving at a judgment of the value of leucocyte counts is the marked discrepancy of opinion concerning their normal range. Swift, Miller, and Boots[57] observed the upper normal limit to be 9,000, a figure identical with my own experience,[56] allowing a 10 per cent deviation.

In this study 85 per cent of the cases showed leucocytosis, its presence ranging from 11 to 100 per cent of the total number of counts. In the entire group 2,413 counts were made, 45 per cent being above 9,000. Leucocytosis was approximately equal in frequency in cases with auricular fibrillation and in those with regular, sinus rhythm (43.9 and 46.1 per cent of the total number of counts in each group, respectively). These figures suggest the presence of an active inflammatory process, probably rheumatic in nature when viewed in conjunction with other observations.

*Temperature.*—Mackie[23] observed that diminished ability to exercise and the onset of cardiac failure were preceded by a rise in temperature and leucocytosis. Swift[11] regarded the temperature curve as probably being "the most important single index of the intensity, the spread, and the persistence of infection." Boas and Schwartz[64] observed bouts of fever in 39 cases, but Findlay[61] thought it of little value as an indication of activity. Though significant, Coombs[17] and Poynton[65] concluded its absence did not necessarily indicate quiescence.

Some of these differences in opinion may be explained by differences in the length of the period of study; whether the temperature was taken by mouth or rectum, and the frequency of measuring. In this study, all

the cases with two exceptions exhibited abnormal temperatures (above 99.6), ranging from one to 38 per cent of the total readings for each individual. In the entire group over 24,000 readings were made, 9.4 per cent being abnormal. The deviations were less in cases with auricular fibrillation than in those with normal sinus rhythm—4.9 and 11.6 per cent of the total readings in each group respectively. Although the elevation in temperature may be only occasional and slight, its significance is apparent when taken in relation to the pulse rate and the leucocyte count. As a sign, however, fever seems to be less valuable than leucocytosis.

*Pulse Rate.*—Findlay[61] thought the pulse rate continued accelerated after prolonged rest in cases not developing cardiac lesions. Coombs[17] also observed it during infectious activity, but was of the opinion that extra-cardiac factors may have occasioned it. When the count was elevated during sleep, Schlesinger[66] regarded it as indicative of active carditis. Allen,[67] Pichon,[20] and Swift[11] believed the sign to be of great value. Swift[11] stressed its importance particularly when out of proportion to the low-grade temperature in the subacute and chronic forms of the disease.

Since there are many factors which elevate the cardiac rate, I have chosen 90 beats per minute as normal and 10 per cent deviation to constitute the normal range.

Tachycardia is a valuable sign of cardiac dysfunction, particularly in this disease. Its significance, however, is limited in auricular fibrillation where digitalis is given, but its persistence after thorough use of this drug is often indicative of the presence of an acute infection. Ninety per cent of the cases with regular sinus rhythm showed tachycardia ranging from 11 to 100 per cent of the total counts. Over 16,000 counts were made, 40 per cent being abnormal.

## SIGNIFICANT SIGNS AND SYMPTOMS

Dyspnea and orthopnea, palpitation, precordial pain, nausea and vomiting, rheumatic polyarthritis, twitching, nodules, muscle and joint pain, hemoptysis, diarrhea, and petechiae, are considered manifestations of activity of infection.

Dyspnea and orthopnea were present in every patient. An increase in dyspnea was very frequently the first clinical indication of beginning acute carditis. The same held true for palpitation. Precordial pain was present in 78 per cent of the cases, ranging from slight precordial distress to attacks of severe pain. Twitching was found in 22 per cent. Muscle and joint pains were both important diagnostic symptoms. In 78 per cent they occurred with considerable frequency. While it cannot be said that these pains were more frequent when rheumatic activity was great, they often appeared during periods of transition from a low to a higher degree of activity. Sometimes they were also

present as a premonitory symptom. Nausea and vomiting, independent of intoxication due to taking digitalis, were present in 75 per cent. They were often seen during acute attacks and were regarded as being indicative of activity. Diarrhea was noticed in five cases, rheumatic polyarthritis in three, and nodules in two. Hemoptysis occurred in six cases. Petechiae, similar to those found by Holtz and Friedman,[68] occurred in 83 per cent. They denote capillary permeability which is probably increased in this disease. The oral and pharyngeal lesions are often difficult to differentiate from those caused by ingestion of coarse food and are, therefore, less significant than those occurring in conjunctivae or skin. The latter appeared in 25 per cent of the cases.

The occurrence of hepatic enlargement, pulmonary râles, and edema was studied; these were undoubtedly the result of partial decompensation due to active carditis. Enlargement of the liver occurred in 80 per cent. It was found in both cases with auricular fibrillation (93 per cent) and those with regular sinus rhythm (75 per cent). Enlargement of the liver was often the only clinical evidence of a slight decompensation. Whether this phenomenon resulted directly from infection of the heart or as the result of mechanical strain, is unknown. Pulmonary râles were noticed in 59 per cent of cases with regular sinus rhythm, and in 87 per cent with auricular fibrillation. Edema was present in 32 per cent, 30 per cent when the rhythm was regular and 40 per cent in auricular fibrillation.

*Valvular Lesions.*—During the course of this study, in 12 patients lesions developed in valves which were previously considered sound. They made their appearance from two to seventy-eight months after the date of admission, the average being 28.5 months. The slow progress of rheumatic infection is indicated by this observation. The length of time required to be certain that this is the course of events greatly limits the opportunity to recognize many cases.

*Electrocardiographic Evidence of Activity.*—The criteria used in this study are those established by Cohn and Swift.[1] Abnormalities found only in Lead III, however, were excluded. A distinction was made be-

TABLE I

TRANSIENT CHANGES IN ELECTROCARDIOGRAMS

| | | |
|---|---|---|
| 1. Increased conduction time | | 14 cases |
| 2. Notching or slurring of the QRS group in 2 or more leads | | 1 case |
| 3. Elevation or depression of R-T interval | | 16 cases |
| 4. T-wave inversion | | 7 cases |
| 5. Irregularities of rhythm | | 24 cases |
| a. Premature auricular beats | 7 cases | |
| b. Premature ventricular beats | 3 cases | |
| c. Nodal premature beats | 2 cases | |
| d. Auricular flutter | 1 case | |
| e. Auricular fibrillation | 9 cases | |
| f. Partial block | 2 cases | |
| g. Bundle-branch block | 1 case | |

tween transient and permanent changes (Tables I and II). Those which may have resulted from taking digitalis were omitted.

TABLE II

PERMANENT CHANGES IN ELECTROCARDIOGRAMS

| | |
|---|---|
| 1. Notching or slurring of the QRS group in 2 or more leads | 50 cases |
| 2. T-wave inversion ($T_1$, $T_2$) | 6 cases |
| 3. Auricular fibrillation | 15 cases |

Transient changes like those described by Cohn and Swift[1] and others,[8, 69-73] were found in 64 per cent of cases with regular sinus rhythm, particularly with regard to the variability of the R-T segment. The observation of Levy and Turner[74] that electrocardiographic abnormalities occurred weeks and months before the onset of acute symptoms, was corroborated in this study. Of the entire group, 90 per cent exhibited permanent changes. In all cases of auricular fibrillation there were in addition notching and slurring in two or more leads.

Auricular fibrillation developed in 9 cases. The view is held by several observers[43-46] and also by McEachern and Baker[75] that under these circumstances the walls of the auricles are invaded by rheumatic infection. High leucocyte counts have been regarded as indicative of this possibility, the rise being 24 to 100 per cent (above 50 per cent in seven cases).

Later histories were obtained in 56 cases (Tables III and IV). High leucocyte counts obtained during observation demonstrated the chronicity of rheumatic activity in this group, and suggested their significance with regard to prognosis. All but 6 patients (10 per cent) either remained stationary or became progressively worse; 26 (46 per cent) died, 18 (65 per cent of the fatalities) as a result of cardiac disease. Patients dying of cardiac failure showed similar evidence of rheumatic activity as those dying of acute carditis. Coexistence of rheumatic activity and subacute bacterial endocarditis (*Streptococcus viridans*) was observed in 3 cases.

TABLE III

FOLLOW-UP DATA THROUGH OCTOBER, 1934* (56 CASES)

| FUNCTIONAL CLASSIFICATION | NUMBER OF CASES | IMPROVED | UNIMPROVED | WORSE | UNCLASSIFIED BECAUSE OF CARDITIS | DIED OF CARDITIS | DIED OF CARDIAC FAILURE | DIED OF SUBACUTE BACTERIAL ENDOCARDITIS | DIED FROM MISCELLANEOUS CAUSES |
|---|---|---|---|---|---|---|---|---|---|
| I | 1 | – | – | 1 | – | – | – | – | – |
| IIA | 14 | 1 | 4 | 3 | 2 | 2 | 2 | – | – |
| IIB | 41 | 5 | 11 | – | 3 | 11 | 3 | 3 | 5 |
| Total Number | | 6 | 15 | 4 | 5 | 13 | 5 | 3 | 5 |

*Based on change in functional classification.

TABLE IV

PER CENT OF ELEVATED LEUCOCYTE COUNTS DURING PERIOD OF OBSERVATION IN RELATION TO FOLLOW-UP DATA

*Improved* (6 cases)
- 2 cases: none
- 1 case : 7 per cent
- 1 case : 30 per cent
- 1 case : 38 per cent
- 1 case : 63 per cent

*Unimproved* (15 cases)
- 3 cases: 0 per cent to 10 per cent
- 4 cases: 22 per cent to 30 per cent
- 4 cases: 50 per cent to 64 per cent
- 4 cases: 74 per cent to 100 per cent

*Worse* (4 cases)
- 1 case : 55 per cent
- 1 case : 67 per cent
- 1 case : 71 per cent
- 1 case : 95 per cent

*Unclassified, carditis* (5 cases)
- 1 case : 26 per cent
- 1 case : 33 per cent
- 1 case : 67 per cent
- 2 cases: 82 per cent

*Died, carditis* (13 cases)
- 4 cases: 3 per cent to 33 per cent
- 5 cases: 56 per cent to 85 per cent
- 4 cases: 100 per cent

*Died, cardiac failure* (5 cases)
- 1 case : 15 per cent
- 1 case : 19 per cent
- 1 case : 25 per cent
- 1 case : 67 per cent
- 1 case : 94 per cent

*Died, subacute bacterial endocarditis* (3 cases)
- 1 case : 19 per cent
- 1 case : 55 per cent
- 1 case : 58 per cent

*Died, miscellaneous causes* (5 cases)
- 1 case : 13 per cent
- 1 case : 23 per cent
- 1 case : 44 per cent
- 1 case : 73 per cent
- 1 case : 100 per cent

## PATHOLOGICAL ANATOMY

Four cases were studied post mortem, 3 dying of acute carditis and one of bronchopneumonia. In the former active inflammation of the various parts of the heart was demonstrated. In the fourth case, one of long standing auricular fibrillation in which activity was considered of little consequence, diffuse scarring but no cellular infiltration was found.

In one of these cases (auricular fibrillation) reactivation of the rheumatic process as demonstrated histologically was associated with signs of decompensation. Great difficulty was encountered in reducing the cardiac rate by adequate use of digitalis. The inability to do so is an important sign of active myocardial inflammation. I have observed this phenomenon repeatedly in cases with auricular fibrillation; it occurs long before the appearance of marked evidence of decompensation. When, therefore, tachycardia persists, increased administration of digitalis must be carried out cautiously as it is otherwise attended by considerable danger in acute carditis. This will be demonstrated in the case reports.

The outstanding signs, symptoms, and laboratory findings characteristic of active rheumatic infection occurring in the group are tabulated in Table V. Some cases showed only three of these features, but many showed considerably more, indicating that all cases had some degree of activity, either during observation or in the interim between the termination of the study and the follow-up period. Leucocytosis

TABLE V

| CASE NUMBER | RHYTHM | AGE | TEMPERATURE | TACHYCARDIA | LEUCOCYTOSIS | NAUSEA AND VOMITTING | DIARRHEA | PRECORDIAL PAIN | TWITCHING | MUSCLE AND JOINT PAIN | POLYARTHRITIS | NODULES | HEMOPTYSIS | PETECHIAL HEMORRHAGES | ADDITIONAL VALVULAR LESIONS | ACUTE CARDITIS | TRANSIENT CHANGES IN ELECTRO-CARDIOGRAMS | POST MORTEM |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | RSR | 16 | + | + | + | + | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | + | + | + | - |
| 2 | RSR | 15 | + | 0 | + | + | 0 | 0 | + | + | 0 | 0 | 0 | 0 | 0 | 0 | + | - |
| 3 | RSR | 17 | + | + | 0 | + | + | 0 | 0 | + | 0 | 0 | 0 | 0 | 0 | 0 | + | - |
| 4 | AF | 17 | + | + | + | - | + | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | - | - |
| 5 | RSR | 15 | + | + | + | + | + | 0 | 0 | + | 0 | 0 | 0 | 0 | 0 | 0 | + | - |
| 6 | RSR | 19 | + | + | + | + | + | 0 | 0 | + | 0 | 0 | 0 | 0 | 0 | 0 | + | - |
| 7 | RSR | 17 | + | + | + | + | + | 0 | 0 | + | 0 | 0 | 0 | + | + | 0 | + | - |
| 8 | AF | 30 | + | + | + | - | + | + | + | + | 0 | 0 | 0 | 0 | 0 | 0 | - | - |
| 9 | RSR | 30 | + | + | + | + | + | 0 | 0 | + | 0 | 0 | 0 | 0 | 0 | 0 | + | - |
| 10 | RSR | 22 | + | + | + | + | + | 0 | 0 | + | 0 | 0 | 0 | 0 | 0 | 0 | + | - |
| 11 | RSR | 17 | + | + | + | + | + | 0 | 0 | + | 0 | 0 | 0 | 0 | 0 | 0 | + | - |
| 12 | AF | 18 | + | + | + | - | + | 0 | 0 | + | 0 | 0 | 0 | 0 | 0 | 0 | - | - |
| 13 | RSR | 17 | + | + | + | + | + | + | + | + | 0 | 0 | 0 | 0 | 0 | 0 | + | - |
| 14 | RSR | 31 | + | + | + | + | + | + | + | + | 0 | 0 | 0 | 0 | 0 | 0 | + | - |
| 15 | RSR | 21 | + | + | + | + | + | + | + | + | 0 | 0 | 0 | 0 | 0 | 0 | + | - |
| 16 | RSR | 16 | + | + | + | + | + | + | + | + | 0 | 0 | 0 | 0 | 0 | 0 | + | - |
| 17 | RSR | 17 | + | + | + | + | + | + | + | + | 0 | 0 | 0 | 0 | 0 | 0 | + | - |
| 18 | RSR | 18 | + | + | + | + | + | + | + | + | 0 | 0 | 0 | 0 | 0 | 0 | + | - |
| 19 | RSR | 25 | + | + | + | - | + | + | + | + | 0 | 0 | 0 | 0 | 0 | 0 | + | - |
| 20 | AF | 20 | 0 | - | + | + | + | + | + | + | + | 0 | 0 | 0 | 0 | 0 | - | - |
| 21 | RSR | 40 | + | + | + | + | + | + | + | + | 0 | 0 | 0 | 0 | 0 | 0 | + | - |
| 22 | RSR | 17 | + | + | + | + | + | + | + | + | 0 | 0 | 0 | 0 | 0 | 0 | + | - |
| 23 | RSR | 17 | + | + | + | + | + | + | + | + | 0 | 0 | 0 | 0 | 0 | 0 | + | - |
| 24 | AF | 18 | + | - | + | - | + | + | + | + | 0 | 0 | 0 | 0 | 0 | 0 | - | - |
| 25 | RSR | 16 | + | 0 | + | + | + | + | + | + | 0 | 0 | 0 | 0 | 0 | 0 | + | - |
| 26 | AF | 30 | + | - | + | - | + | + | + | + | 0 | 0 | 0 | 0 | 0 | 0 | - | - |
| 27 | RSR | 24 | + | + | + | + | + | + | + | + | 0 | 0 | 0 | 0 | 0 | 0 | + | - |
| 28 | RSR | 21 | + | + | + | + | + | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | + | - |
| 29 | RSR | 20 | + | + | + | + | + | + | + | + | 0 | 0 | 0 | 0 | 0 | 0 | + | - |
| 30 | RSR | 17 | + | + | + | + | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | + | - |

+ = present  0 = absent  - = indeterminate

TABLE V—CONT'D

| CASE NUMBER | RHYTHM | AGE | TEMPERATURE | TACHYCARDIA | LEUCOCYTOSIS | NAUSEA AND VOMITTING | DIARRHEA | PRECORDIAL PAIN | TWITCHING | MUSCLE AND JOINT PAIN | POLYARTHRITIS | NODULES | HEMOPTYSIS | PETECHIAL HEMORRHAGES | ADDITIONAL VALVULAR LESIONS | ACUTE CARDITIS | TRANSIENT CHANGES IN ELECTRO-CARDIOGRAMS | POST MORTEM |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 31 | RSR | 19 | + | + | + | + | 0 | + | 0 | + | 0 | 0 | 0 | + | 0 | 0 | + | - |
| 32 | RSR | 22 | + | 0 | + | + | 0 | + | 0 | 0 | 0 | 0 | 0 | 0 | 0 | + | + | - |
| 33 | RSR | 21 | + | + | + | + | 0 | + | 0 | + | 0 | 0 | 0 | + | 0 | 0 | + | - |
| 34 | RSR | 25 | + | + | + | + | 0 | + | 0 | 0 | 0 | 0 | 0 | 0 | 0 | + | + | - |
| 35 | RSR | 17 | + | + | + | + | 0 | + | 0 | + | 0 | 0 | 0 | 0 | 0 | 0 | + | - |
| 36 | AF | 16 | + | - | + | - | + | + | 0 | 0 | 0 | + | 0 | + | 0 | + | - | - |
| 37 | RSR | 16 | + | + | + | 0 | 0 | + | 0 | + | 0 | 0 | 0 | 0 | 0 | 0 | + | - |
| 38 | RSR | 17 | + | + | 0 | 0 | 0 | 0 | 0 | + | 0 | 0 | 0 | 0 | 0 | 0 | - | - |
| 39 | AF | 18 | + | - | + | - | 0 | + | 0 | + | 0 | 0 | 0 | 0 | 0 | 0 | + | - |
| 40 | RSR | 19 | + | + | + | + | + | + | 0 | + | 0 | 0 | 0 | 0 | 0 | + | + | - |
| 41 | RSR | 24 | 0 | + | 0 | + | 0 | + | 0 | + | 0 | 0 | 0 | 0 | 0 | 0 | + | - |
| 42 | RSR | 17 | + | + | + | + | + | 0 | 0 | + | 0 | 0 | 0 | 0 | - | 0 | + | - |
| 43 | RSR | 23 | + | + | + | + | 0 | + | 0 | + | 0 | 0 | 0 | 0 | 0 | 0 | + | - |
| 44 | AF | 36 | + | - | + | - | 0 | + | 0 | + | 0 | 0 | 0 | 0 | 0 | 0 | + | - |
| 45 | AF | 28 | - | - | + | - | 0 | + | + | + | 0 | 0 | 0 | 0 | 0 | + | + | - |
| 46 | RSR | 17 | + | + | + | + | 0 | + | 0 | + | 0 | 0 | + | + | + | 0 | + | - |
| 47 | RSR | 17 | + | + | + | 0 | 0 | + | 0 | + | 0 | 0 | + | + | + | 0 | + | - |
| 48 | RSR | 17 | + | + | + | + | 0 | + | + | + | 0 | 0 | + | + | + | 0 | + | - |
| 49 | AF | 28 | + | - | + | - | 0 | + | 0 | + | 0 | 0 | 0 | 0 | 0 | 0 | + | - |
| 50 | RSR | 26 | 0 | + | + | + | + | + | 0 | + | 0 | 0 | + | + | 0 | + | + | - |
| 51 | AF | 20 | + | - | + | - | 0 | + | 0 | + | + | 0 | 0 | 0 | + | 0 | + | - |
| 52 | RSR | 16 | + | + | + | 0 | 0 | 0 | + | + | 0 | 0 | 0 | 0 | 0 | 0 | + | - |
| 53 | AF | 24 | + | - | 0 | - | 0 | + | 0 | + | 0 | 0 | 0 | 0 | + | 0 | + | + |
| 54 | RSR | 17 | + | + | + | + | 0 | + | + | + | 0 | 0 | 0 | 0 | 0 | 0 | + | - |
| 55 | RSR | 23 | + | + | + | + | 0 | + | + | + | 0 | 0 | 0 | + | 0 | 0 | + | - |
| 56 | RSR | 27 | + | + | + | + | 0 | + | 0 | + | 0 | 0 | 0 | + | 0 | 0 | + | - |
| 57 | AF | 44 | - | - | + | - | 0 | + | 0 | + | 0 | 0 | 0 | 0 | 0 | 0 | - | - |
| 58 | AF | 17 | + | - | + | - | 0 | + | 0 | + | 0 | 0 | + | + | 0 | + | - | - |
| 59 | RSR | 18 | + | + | + | + | 0 | + | 0 | + | 0 | 0 | 0 | 0 | + | + | 0 | - |

+ = present 0 = absent - = indeterminate

was by far the most prominent sign in recognizing rheumatic activity regardless of rhythm; muscle and joint pain, and precordial pain were next in importance; tachycardia and transient changes in the electrocardiogram were very valuable signs in the group with regular sinus rhythm. Although abnormal temperature occurred in all but one case, it did not occur with sufficient regularity in many to be considered as important as those signs already mentioned.

### CASE REPORTS

Several cases, both of regular sinus rhythm and of auricular fibrillation, exhibiting various types of activity are discussed in detail in the following case reports. Although Pichon,[20] on the basis of clinical observations, classified rheumatic activity into two types, (a) an evolutive or chronic form (not a cicatricial one in which the process has stopped), and (b) acute pancarditis, it is my opinion that the difference is one of degree only.

CASE 30.—E. L., aged seventeen years, was admitted to the Cardiac Shop Sept. 5, 1930. The diagnosis was rheumatic mitral stenosis and insufficiency, enlarged heart; the rhythm was regular, and her functional classification IIA. Cardiac symptoms were observed by the patient one year prior to the onset of rheumatic fever. Her illness began with an attack of tonsillitis followed by rheumatic polyarthritis in the Spring of 1930. Fever, tachycardia, and leucocytosis persisted throughout the period of observation (Fig. 1). Bouts of acute carditis occurred in December, 1930, and October, 1931: the first was associated with symptoms of nausea, vomiting, increasing dyspnea, orthopnea and cough, the second was preceded by an upper respiratory infection. There were periods, which often coincided with increased cardiac reserve, when the leucocyte curve approached the normal level, but quiescence was never attained. Cardiac reserve diminished when rheumatic activity increased, as shown by the two bouts of acute carditis. She was observed until Jan. 25, 1932, a period of seventeen months. During July and August, 1934, "she was confined to a hospital. Diagnosis: *active carditis,* mitral stenosis and insufficiency, *aortic insufficiency,* regular sinus rhythm, *no classification because of rheumatic activity.*"

CASE 36.—J. O'D., aged sixteen years, was admitted to the Cardiac Shop May 22, 1929. The diagnosis was rheumatic mitral stenosis and insufficiency, enlarged heart, auricular fibrillation, Class IIB. At the age of three years, tonsillectomy was performed. The presence of heart disease was discovered at the age of six years during a routine physical examination. At twelve years, she suffered an attack of rheumatic polyarthritis, when cardiac symptoms were first experienced. Low-grade fever, occasional periods of tachycardia, pulse deficit, and persistent leucocytosis were present (Fig. 2). Frequent bouts of acute carditis made the problem of giving digitalis difficult. The maintenance dose was not increased so that toxic manifestations, often similar to the symptoms of the disease, might be avoided. Rest in bed was often sufficient to bring about a state of improvement. The first bout of carditis observed occurred in September, 1929, and was associated with diarrhea, vomiting and palpitation. The second, December, 1929, preceded by an upper respiratory infection, was associated with slight edema of the ankles. The third, October, 1930, was associated with pains in the knees and cyanosis of the lips. The fourth occurred

in February, 1931, accompanied by pains in her joints. Rheumatic nodules were noticed in March, 1931. The fifth bout occurred in April, 1931. After treatment in a hospital and care in a convalescent home the patient returned in August, 1931, much improved. She was studied until Jan. 25, 1932, a period of thirty-two months. On March 5, 1934, *"her left hand was swollen and painful, nodules appeared on ankles and elbows.* The diagnosis was mitral stenosis and insufficiency, auricular fibrillation, *not classified because of rheumatic activity."*

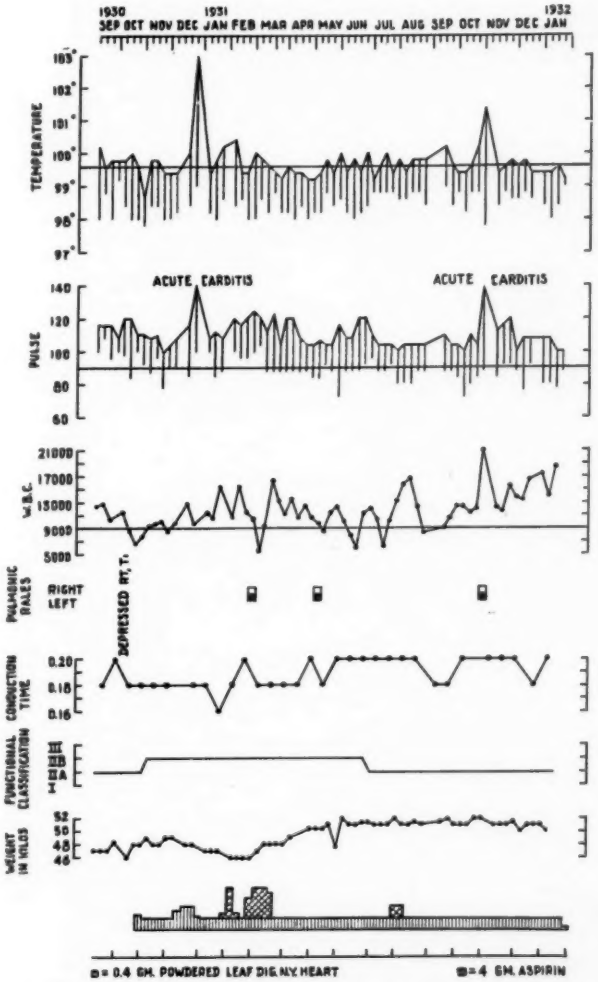


Fig. 1.—Each space indicated on the top contains the data collected during one week. The high and low pulse counts and temperature readings for each week are indicated by vertical lines. The highest weekly pulse counts and temperature readings are joined by continuous lines. In cases of auricular fibrillation the pulse deficit is represented by shaded areas, its absence by a single continuous line. The weekly white cell count is recorded by connecting lines.

These two cases illustrate a continuous type of activity lasting for years, with bouts of acute carditis occurring with equal intensity both when the rhythm was regular and during auricular fibrillation. The bouts were probably accentuated manifestations of a preexisting active rheumatic state.

CASE 6.—H. B., aged nineteen years, was admitted to the Cardiac Shop Nov. 3, 1928. The diagnosis was rheumatic mitral stenosis and insufficiency, enlarged heart, regular sinus rhythm, Class IIB. Tonsillectomy was performed at six years of age. She was seized with chorea at eleven years, when the presence of heart disease was discovered. Cardiac symptoms were first observed by the patient the following year during a period of fever. Persistent low-grade fever, tachycardia and leucocytosis were observed (Fig. 3). The first bout of acute carditis occurred in April, 1929,

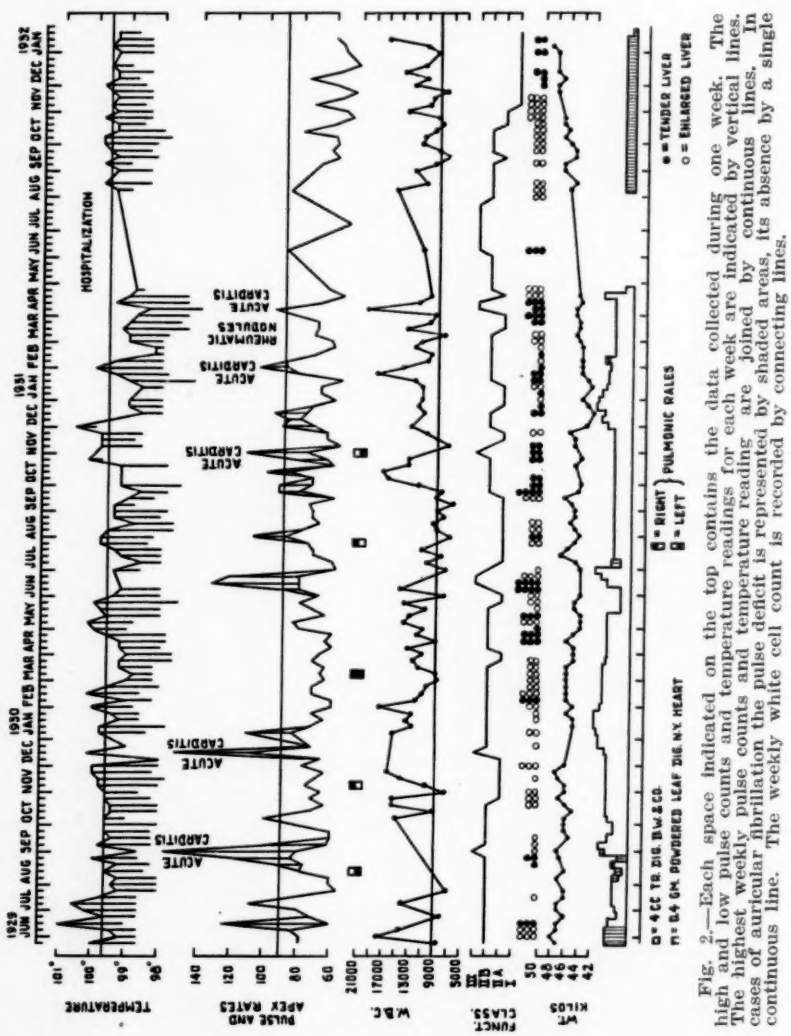
1929 JUN JUL AUG SEP OCT NOV DEC 1930 JAN FEB MAR APR MAY JUN JUL AUG SEP OCT NOV DEC 1931 JAN FEB MAR APR MAY JUN JUL AUG SEP OCT NOV DEC 1932 JAN
HOSPITALIZATION
ACUTE CARDITIS
RHEUMATIC NODULES
TEMPERATURE
PULSE AND APEX RATES
W.B.C.
FUNCT. CLASS.
WT. KILOS
= RIGHT
= LEFT
PULMONIC RALES
= TENDER LIVER
= ENLARGED LIVER
= 4 CC TR. DIG. B.W.&CO.
= 0.4 GM. POWDERED LEAF DIG. N.Y. HEART

Fig. 2.—Each space indicated on the top contains the data collected during one week. The high and low pulse counts and temperature readings for each week are indicated by vertical lines. The highest weekly pulse counts and temperature reading are joined by continuous lines. In cases of auricular fibrillation the pulse deficit is represented by shaded areas, its absence by a single continuous line. The weekly white cell count is recorded by connecting lines.

associated with increase in the degree of her cardiac symptoms and the first appearance of premature auricular beats. From September, 1929, through November, 1929, she was confined to her home during the second attack of acute carditis. In December, 1929 she contracted acute bronchopneumonia. Premature auricular beats began to increase in number and in the latter part of February, 1930, gallop rhythm was observed. Digitalis was given, but the persistence of the symptoms necessitated complete rest. In March, 1930, slight pitting edema of the legs was noticed. Dyspnea, nausea, vomiting, and diarrhea were also present; they were at-

tributed to acute carditis and not to digitalis intoxication. On Aug. 14, 1930, during the third period of acute carditis, auricular fibrillation supervened. In May, 1931, following severe infection of the upper respiratory tract, a fourth bout occurred associated with cough and vomiting. The temperature, apex rate, and leucocyte counts

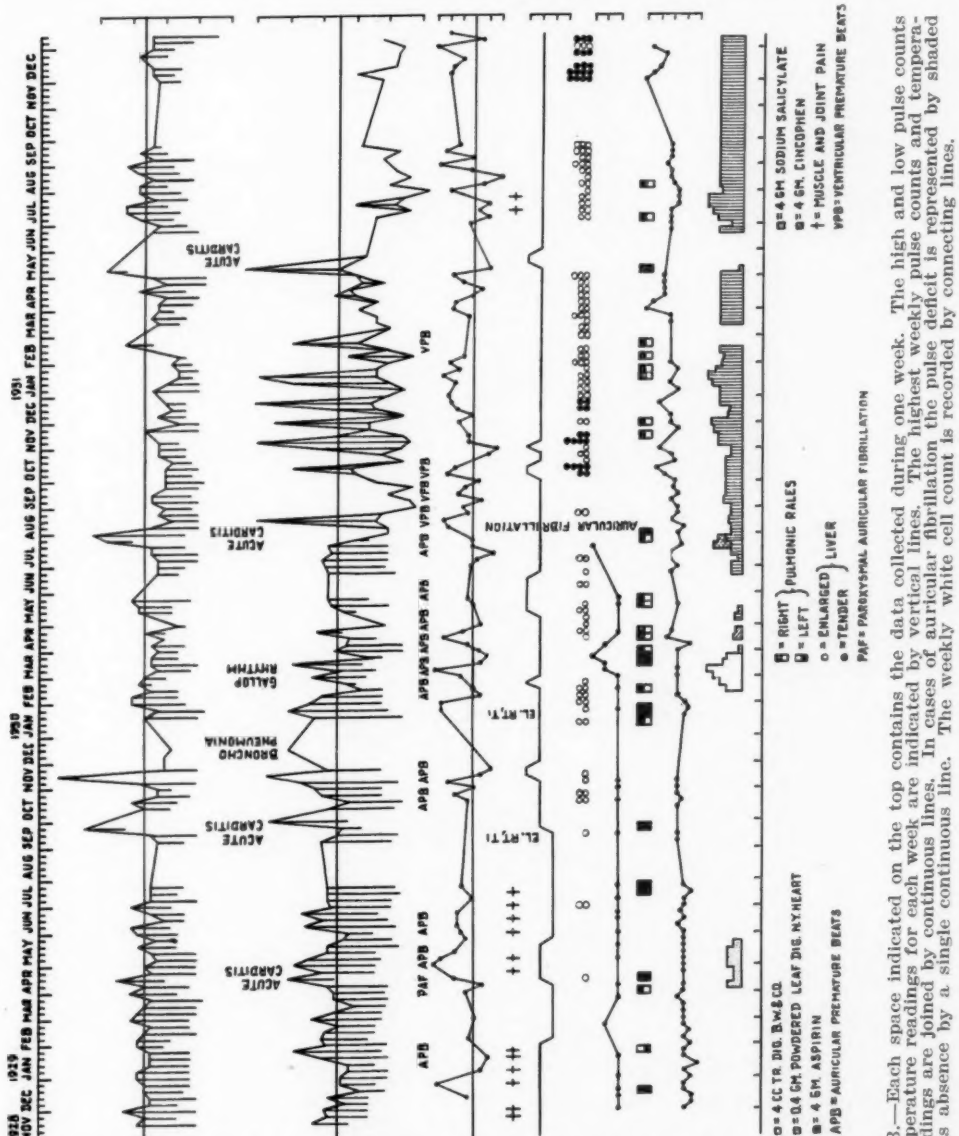
1928 1929 1930 1931
NOV DEC JAN FEB MAR APR MAY JUN JUL AUG SEP OCT NOV DEC JAN FEB MAR APR MAY JUN JUL AUG SEP OCT NOV DEC
TEMPERATURE
PULSE AND APEX RATES
W.B.C.
FUNCT. CLASS.
CONDUCT. TIME
WT. KILOS
ACUTE CARDITIS
BRONCHO PNEUMONIA
GALLOP RHYTHM
APB
PAF
VPB
AURICULAR FIBRILLATION
EL. RT. T1
□ = 4 CC TR. DIG. B.W.&CO.
□ = 0.4 GM. POWDERED LEAF DIG. NY HEART
□ = 4 GM. ASPIRIN
APB = AURICULAR PREMATURE BEATS
□ = RIGHT } PULMONIC RALES
□ = LEFT }
○ = ENLARGED } LIVER
● = TENDER
PAF = PAROXYSMAL AURICULAR FIBRILLATION
□ = 4 GM. SODIUM SALICYLATE
□ = 4 GM. CINCOPHEN
† = MUSCLE AND JOINT PAIN
VPB = VENTRICULAR PREMATURE BEATS

Fig. 3.—Each space indicated on the top contains the data collected during one week. The high and low pulse counts and temperature readings for each week are indicated by vertical lines. The highest weekly pulse counts and temperature readings are joined by continuous lines. In cases of auricular fibrillation the pulse deficit is represented by shaded areas, its absence by a single continuous line. The weekly white cell count is recorded by connecting lines.

rose, and the severity of her cardiac symptoms increased. The patient was confined to bed in a hospital for one month. In October, 1931, she was sent to a convalescent home for two months and returned much improved. She was observed until Jan. 25, 1932, a period of thirty-nine months. On Oct. 8, 1934, the diagnosis was "mitral stenosis and insufficiency, *aortic insufficiency, auricular fibrillation,* Class IIB."

In this case, the occurrence of auricular fibrillation is exhibited during a period of acute carditis and the continuance of rheumatic activity in the same state of intensity after the change of rhythm.

CASE 25.—S. K., aged sixteen years, was admitted to the Cardiac Shop Jan. 13, 1930. The diagnosis was rheumatic mitral stenosis and insufficiency, enlarged heart, regular sinus rhythm, Class IIB. There was no history of polyarthritis, chorea, or tonsillitis. Her tonsils were removed at six and at thirteen years of age. The existence of heart disease was discovered at the age of eight years. The first cardiac symptoms, together with chills, fever, palpitation, and dyspnea, appeared in 1929. The temperature, pulse, and leucocyte curves showed cyclic periods of fever, tachycardia, and leucocytosis (Fig. 4). An elevation of the three curves during July, 1930,

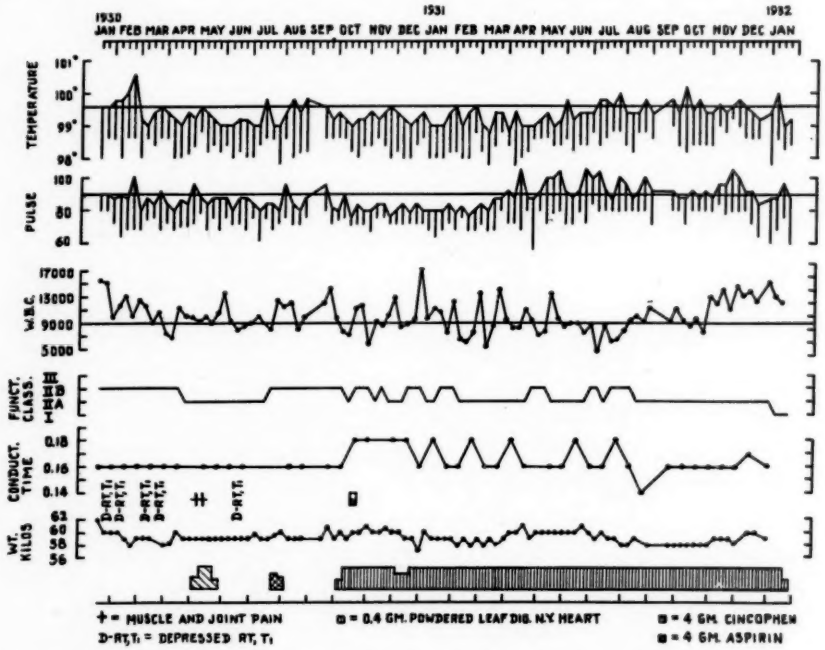


Fig. 4.—Each space indicated on the top contains the data collected during one week. The high and low pulse counts and temperature readings for each week are indicated by vertical lines. The highest weekly pulse counts and temperature readings are joined by continuous lines. In cases of auricular fibrillation the pulse deficit is represented by shaded areas, its absence by a single continuous line. The weekly white cell count is recorded by connecting lines.

was associated with increased dyspnea. The symptoms, however, did not reach sufficient proportions to be considered those of acute carditis. Regardless of improvement (Class I) during January, 1932, the evidence revealed persistent rheumatic activity. She was observed until Jan. 25, 1932, a period of twenty-four months. On Oct. 22, 1934, she complained of "palpitation, dyspnea, orthopnea, occasional cardiac pain, feeling of oppression over precordium. The diagnosis was rheumatic mitral stenosis and insufficiency, *auricular fibrillation*, Class IIB."

CASE 12.—J. DeJ., aged eighteen years, was admitted to the Cardiac Shop July 11, 1929. The diagnosis was rheumatic mitral stenosis and insufficiency, enlarged heart, auricular fibrillation, Class IIA. There was no history of polyarthritis or

chorea. The presence of heart disease was discovered at eleven years. An attack of tonsillitis had occurred at twelve years; the tonsils were removed at thirteen. Cardiac symptoms began to be noticed at thirteen years, when irregular palpitation was felt and digitalis was given. Irregular periods were observed of low-grade fever and leucocytosis, the latter being the more pronounced (Fig. 5). The cardiac rate was lowered by taking digitalis. The course of this patient was complicated by the occurrence of amenorrhea from May until August, 1931, and later by metrorrhagia,

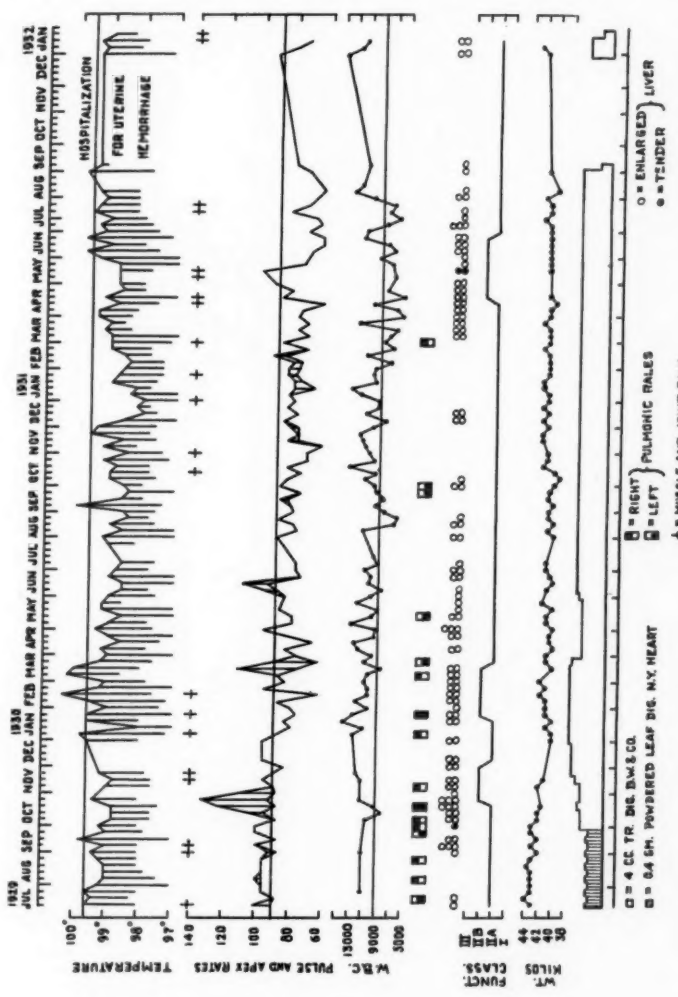
1929
JUL AUG SEP OCT NOV DEC JAN FEB MAR APR MAY JUN JUL AUG SEP OCT NOV DEC JAN FEB MAR APR MAY JUN JUL AUG SEP OCT NOV DEC JAN
1930
1931
1932
HOSPITALIZATION
FOR UTERINE HEMORRHAGE
TEMPERATURE
PULSE AND APEX RATES
W.B.C.
FUNCT. CLASS
WT. KILOS
□ = 4 CC TR. DIG. B.W.& CO.
□ = 0.4 GM. POWDERED LEAF DIG. N.Y. HEART
□ = RIGHT
□ = LEFT
PULMONIC RALES
o = ENLARGED
• = TENDER
LIVER
+ = MUSCLE AND JOINT PAIN

Fig. 5.—Each space indicated on the top contains the data collected during one week. The high and low pulse counts and temperature readings for each week are indicated by vertical lines. The highest weekly pulse counts and temperature readings are joined by continuous lines. In cases of auricular fibrillation the pulse deficit is represented by shaded areas, its absence by a single continuous line. The weekly white cell count is recorded by connecting lines.

lasting three weeks and causing secondary anemia, severe enough to necessitate transfusion of blood. She was observed until Jan. 25, 1932, a period of thirty-one months. On Oct. 16, 1934, she was "feeling ill, complaining of nausea, fatigue, dyspnea, cough, and palpitation. The diagnosis was rheumatic mitral stenosis and insufficiency, auricular fibrillation, Class IIB."

These two cases presented the same degree of rheumatic activity when the rhythm was regular and when auricular fibrillation was pres-

ent. There was evidence of alternating rheumatic activity and latency. Cardiac reserve was not so much diminished nor did the activity assume such proportions as would suggest the presence of acute carditis. The use of digitalis was also a much simpler problem than in the previous group.

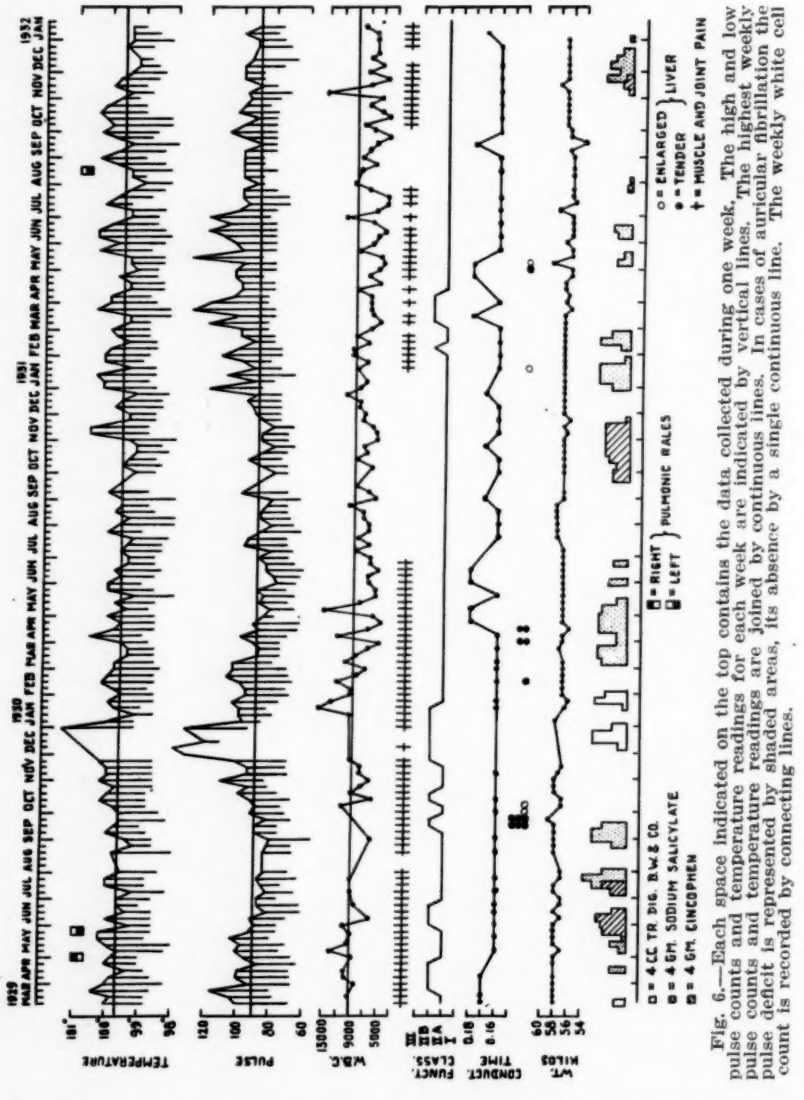
1929 FEB APR MAY JUN JUL AUG SEP OCT NOV DEC JAN FEB MAR APR MAY JUN JUL AUG SEP OCT NOV DEC JAN 1930 FEB MAR APR MAY JUN JUL AUG SEP OCT NOV DEC JAN 1931 FEB MAR APR MAY JUN JUL AUG SEP OCT NOV DEC JAN 1932
TEMPERATURE
PULSE
W.B.C.
FUNCT. CLASS
CONDUCT. TIME
WT. KILOS
□ = 4 CC TR. DIG. B.W.& CO.
▨ = 4 GM. SODIUM SALICYLATE
▩ = 4 GM. CINCOPHEN
□ = RIGHT ▨ = LEFT PULMONIC RALES
○ = ENLARGED ● = TENDER + = MUSCLE AND JOINT PAIN LIVER

Fig. 6.—Each space indicated on the top contains the data collected during one week. The high and low pulse counts and temperature readings for each week are indicated by vertical lines. The highest weekly pulse counts and temperature readings are joined by continuous lines. In cases of auricular fibrillation the pulse deficit is represented by shaded areas, its absence by a single continuous line. The weekly white cell count is recorded by connecting lines.

CASE 55.—G. S., aged twenty-three years, was admitted to the Cardiac Shop March 12, 1929. The diagnosis was rheumatic mitral stenosis and insufficiency, enlarged heart, regular sinus rhythm, Class IIA. She suffered an attack of tonsillitis at seventeen years, the tonsils were removed at eighteen, heart disease was discovered at nineteen with the onset of cardiac symptoms; an attack of rheumatic polyarthritis occurred at twenty-one. The pulse rate, temperature, and leucocyte curves ran a more or less parallel course, being elevated from March, 1929, to May, 1930 (Fig. 6). The

leucocyte curve then reached a normal level with only a rare count above 9,000. The other curves fluctuated, however, showing occasional periods of tachycardia and slight fever, particularly between November, 1930, and the termination of the study. The chief complaints were frequent pains in muscles and joints. During December, 1930, the severity of her cardiac symptoms increased. She was observed until Jan. 25, 1932, a period of thirty-four months. On Oct. 8, 1934, she was "feeling ill, complained of pains in arms and legs, fatigue, dyspnea, occasional palpitation. The diagnosis was rheumatic mitral stenosis and insufficiency, regular sinus rhythm, Class IIA."

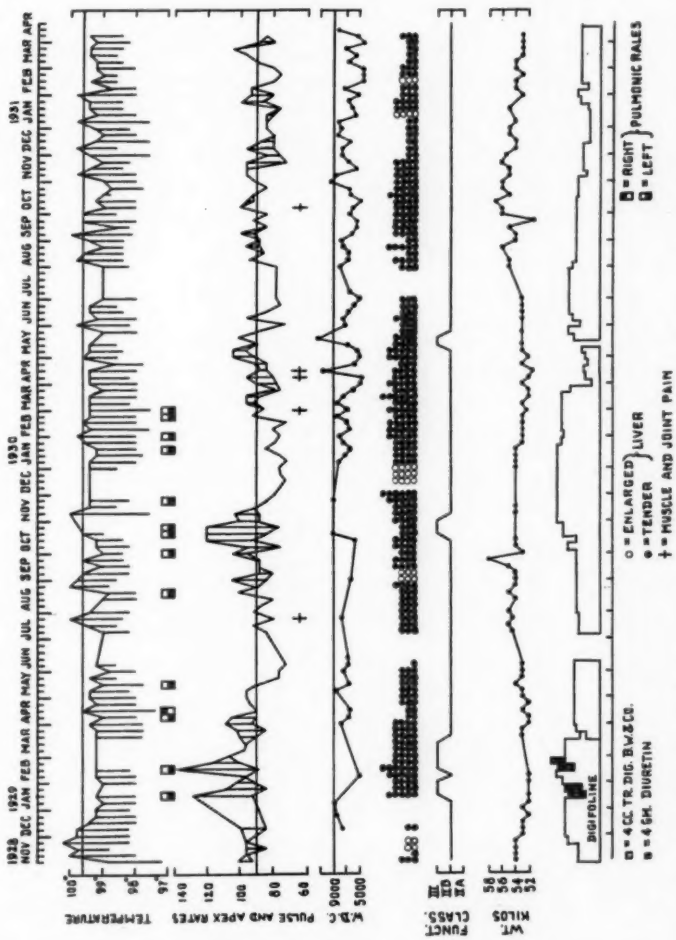
1928 1929 1930 1931
NOV DEC JAN FEB MAR APR MAY JUN JUL AUG SEP OCT NOV DEC JAN FEB MAR APR MAY JUN JUL AUG SEP OCT NOV DEC JAN FEB MAR APR
TEMPERATURE
PULSE AND APEX RATES
W.B.C.
FUNCT. CLASS.
WT. KILOS
O = ENLARGED } LIVER
● = TENDER
+ = MUSCLE AND JOINT PAIN
□ = RIGHT } PULMONIC RALES
■ = LEFT
□ = 4 CC. TR. DIG. B.W.&CO.
■ = 4 GM. DIURETIN
DIGIFOLINE

Fig. 7.—Each space indicated on the top contains the data collected during one week. The high and low pulse counts and temperature readings for each week are indicated by vertical lines. The highest weekly pulse counts and temperature readings are joined by continuous lines. In cases of auricular fibrillation the pulse deficit is represented by shaded areas, its absence by a single continuous line. The weekly white cell count is recorded by connecting lines.

This case is an example of the type in which long periods of quiescence are interrupted by periods of slight rheumatic activity, more apparent from the pulse and temperature curves than from the leucocyte curve.

CASE 8.—C. B., aged thirty years, was admitted to the Cardiac Shop Nov. 3, 1928. The diagnosis was rheumatic mitral stenosis and insufficiency, enlarged heart, auricular fibrillation, Class IIB. An attack of rheumatic polyarthritis occurred at the age of twenty, when the existence of heart disease was discovered. Cardiac symptoms appeared first at twenty-three, with the onset of irregular palpitation and decom-

pensation. Throughout the entire course of study, a few leucocyte counts only were above 9,000 (Fig. 7). There was an occasional rise in temperature not associated with pulse deficits. She complained at times of muscle and joint pains. The chief difficulty in treatment consisted in finding the correct dose of digitalis. She was observed until April 17, 1931, a period of thirty months. On Aug. 27, 1934, "the diagnosis was rheumatic mitral stenosis and insufficiency, *aortic insufficiency*, auricular fibrillation, Class IIB."

This case illustrates a grade of rheumatic activity so low that its presence cannot be demonstrated by usual methods. Nevertheless, after a period of six years, the involvement of an additional valve became apparent. In all probability the process was fibrotic, slow in growth, rather than inflammatory.

In the next case, rheumatic activity was known to exist for three months prior to the onset of cardiac symptoms. It is included to show the compatibility of rheumatic activity with normal physical capacity.

CASE 13.—L. D., aged seventeen years, was admitted to the Cardiac Shop Oct. 7, 1931. The diagnosis was rheumatic mitral stenosis and insufficiency, aortic stenosis and insufficiency, enlarged heart, regular sinus rhythm, Class I. An attack of tonsillitis occurred at nine years, heart disease was discovered at ten years, and an attack of chorea took place at eleven years. The history of this case suggests an intermittent type of activity. Cardiac symptoms first appeared at the end of the study. She was observed until Jan. 15, 1932, a period of three months. On Aug. 16, 1934, a history was obtained of "*epistaxis, hemoptysis, palpitation, precordial pain, pain in elbows and wrists.* She was sleeping on three pillows. The diagnosis was rheumatic mitral stenosis and insufficiency, aortic stenosis and insufficiency, *sinus tachycardia, Class IIB.*"

This is the type of case which explains the presence of rheumatic inflammation frequently found post mortem when it was not suspected during life.

The chronicity of infection, exhibited by these cases emphasizes the similarity between chronic rheumatic cardiac disease and chronic pulmonary tuberculosis, frequently referred to by other observers.[17, 76] In both maladies recrudescence may be expected even in the absence of objective signs of activity. Evidence suggested that rheumatic activity ranged from being quiescent, with occasional periods of recrudescence, to being continuous, with bouts of acute carditis, leading in each instance to further damage to the heart. The present use of the term "carditis," limited as it is to frankly acute exacerbations with obvious signs and symptoms, is erroneous and misleading. The data reveal unquestionable evidence of mild acute carditis long before a typical "attack" supervenes.

## SUMMARY

1. Information was collected on 59 ambulatory cases of chronic rheumatic cardiac disease by obtaining at suitable intervals, histories, symptoms, leucocyte counts, pulse rates, measurements of temperature, physical examinations, electrocardiograms, x-ray photographs of the

heart, and post-mortem reports. The group consisted of women between the ages of fifteen and forty-four years who were studied for a period of one to thirty-nine months, the average being 13.7 months.

2. Rheumatic infection was probably active in each case either during observation or later.

3. The most valuable single procedure for ascertaining the presence of rheumatic activity was the leucocyte count. Leucocytosis occurred in 85 per cent of the cases, its presence ranging from 11 to 100 per cent of the total number of counts.

4. In some cases the rheumatic process appeared to be (a) either relatively quiescent or only slightly active, (b) in others, periods of inactivity alternated with others of activity, and (c) finally there were those in which activity was more or less continuous. These types occurred with equal frequency whether the rhythm was regular or there was auricular fibrillation.

5. Patients manifesting frank signs and symptoms of acute carditis showed evidence of having had a preexisting active rheumatic state.

6. Whether death occurred as the result of cardiac failure or of acute carditis, similar evidence of rheumatic activity was found.

7. In three patients rheumatic activity and subacute bacterial endocarditis coexisted.

8. The regular sinus rhythm gave way to auricular fibrillation in nine cases. In each instance the irregularity supervened during periods of rheumatic activity.

9. In several cases, rheumatic activity continued for several years, leading to progressive cardiac damage and diminished cardiac reserve.

10. In certain cases rheumatic activity is at times compatible with normal cardiac reserve.

## CONCLUSION

In this study it is shown that in many adult cases of rheumatic heart disease prolonged and progressive active infection persists, sometimes so mild as to be scarcely detectable, but sometimes exhibiting high grades of severity.

## REFERENCES

1. Cohn, A. E., and Swift, H. F.: J. Exper. Med. 39: 1, 1924.
2. Swift, H. F.: Transactions of the Medical and Chirurgical Faculty, 1925-1929. Trimble Lecture, p. 30.
3. Mackie, T. T.: Am. Heart J. 3: 31, 1927.
4. Bach, F.: Rheumatism: Its Significance in Youth and Middle Age, London, 1930, P. S. King & Son, Ltd.
5. Newman, G.: Proceedings of a Conference of Rheumatic Diseases, Bath, 1928, Bath City Council.
6. Poynton, F. J.: Brit. M. J. 2: 788, 1925.
7. Askins, R. A.: Brit. M. J. 2: 791, 1925.
8. Poynton, F. J., and Schlesinger, B.: Recent Advances in the Study of Rheumatism, Philadelphia, 1931, P. Blakiston's Son & Co.
9. Acute Rheumatism in Children and Its Relation to Heart Disease, London, 1927, Ministry of Health.
10. Wyckoff, J., and Lingg, C.: Am. Heart J. 1: 446, 1926.

11. Swift, H. F.: Rheumatic Fever. Nelson's Loose Leaf Medicine, Vol. I. New York, 1931, Thomas Nelson & Sons, p. 401.
12. Paul, J. R.: The Epidemiology of Rheumatic Fever, New York, 1930, Metropolitan Life Insurance Co.
13. Swift, H. F.: Am. Heart J. 6: 625, 1931.
14. Poynton, F. J., and Paine, A.: Researches on Rheumatism, New York, 1914, The Macmillan Company.
15. Epstein, J.: Arch. Pediat. 48: 635, 1931.
16. Thomson, A. P.: Proceedings of a Conference of Rheumatic Diseases, Bath, 1928, Bath City Council.
17. Coombs, C. F.: Rheumatic Heart Disease, New York, 1924, William Wood & Company.
18. Clawson, B. J.: J. Infect. Dis. 49: 90, 1931.
19. Poynton, F. J., Paterson, D., and Spence, J. C.: Lancet, 2: 1086, 1920.
20. Pichon, J. B. E.: Le Rhumatisme Cardiaque Évolutif et son Traitement, Paris, 1924.
21. Gibson: Quoted in Acute Rheumatism in Children and Its Relation to Heart Disease, London, 1927, Ministry of Health.
22. Southerland: Quoted in Acute Rheumatism in Children and Its Relation to Heart Disease, London, 1927, Ministry of Health.
23. Mackie, T. T.: Am. J. M. Sc. 172: 199, 1926.
24. Swift, H. F.: J. A. M. A. 92: 2071, 1929.
25. Swift, H. F., Derick, C. L., and Hitchcock, C. H.: Transactions of the Association of American Physicians 43: 192, 1928.
26. Swift, H. F., Hitchcock, C. H., Derick, C. L., and McEwen, C.: Am. J. M. Sc. 181: 1, 1931.
27. Wilson, M. G., and Swift, H. F.: Am. J. Dis. Child. 42: 42, 1931.
28. Small, J. C.: Am. J. M. Sc. 175: 638, 1928.
29. McCulloch: Quoted by Bach, F., Rheumatism: Its Significance in Youth and Middle Age, London, 1930, P. S. King & Son, Ltd.
30. Poynton, F. J.: Introduction to Coombs, C. F., Rheumatic Heart Disease, New York, 1924, William Wood & Company.
31. Pitcairn: Quoted by Cohn, A. E., and Swift, H. F., J. Exper. Med. 39: 1, 1924.
32. Wells: Quoted by Cohn, A. E., and Swift, H. F., J. Exper. Med. 39: 1, 1924.
33. Henoch: Quoted by Pichon, J. B. E., Le Rhumatisme Cardiaque Évolutif et son Traitement, Paris, 1924.
34. Bard: Quoted by Pichon, J. B. E., Le Rhumatisme Cardiaque Évolutif et son Traitement, Paris, 1924.
35. Bouillaud and Bard: Quoted by Pichon, J. B. E., Le Rhumatisme Cardiaque Évolutif et son Traitement, Paris, 1924.
36. Rothschild, M. A., Kugel, M. A., and Gross, L.: Am. Heart J. 9: 586, 1934.
37. Sacks, B.: Am. Heart J. 1: 750, 1926.
38. Davis, D., and Weiss, S.: Am. Heart J. 8: 146, 1931.
39. Leary, T.: Quoted by Davis, D., and Weiss, S., Am. Heart J. 8: 146, 1931.
40. Clawson, J.: Arch. Path. 8: 664, 1929.
41. Pappenheimer, A. M., and von Glahn, W. C.: Am. J. Path. 2: 15, 1926.
42. Kugel, M. A., and Epstein, E. Z.: Arch. Path. 6: 247, 1928.
43. Perry, C. B.: Quart. J. Med. 23: 241, 1930.
44. MacCallum, W. G.: Bull. Johns Hopkins Hosp. 35: 329, 1924.
45. MacCallum, W. G.: J. A. M. A. 21: 1545, 1925.
46. Von Glahn, W. C.: Am. J. Path. 2: 1, 1926.
47. Pappenheimer, A. M., and von Glahn, W. C.: Am. J. Path. 3: 583, 1927.
48. Zeek, P.: Am. J. M. Sc. 184: 350, 1932.
49. Slater, S. R.: Am. J. M. Sc. 179: 22, 1930.
50. Slater, S. R.: Am. J. M. Sc. 181: 203, 1931.
51. Ash, R.: Am. J. Dis. Child. 52: 280, 1936.
52. Wilson, M. G., and Koppel, M.: Am. J. Dis. Child. 32: 46, 1926.
53. Swift, H. F.: Am. Heart J. 6: 625, 1931.
54. Coburn, A. F.: The Factor of Infection in the Rheumatic State, Baltimore, 1931, Williams & Wilkins Company.
55. Criteria for the Classification and Diagnosis of Heart Disease, ed. 3, New York, 1935, The New York Tuberculosis and Health Association.
56. Juster, I. R.: J. Lab. and Clin. Med. 21: 376, 1936.
57. Swift, H. F., Miller, C. P., and Boots, R.: J. Clin. Investigation 1: 197, 1924.
58. Thayer, quoted by East, C. F. T., and Bain, C. W. C.: Recent Advances in Cardiology, Philadelphia, 1929, P. Blakiston's Son & Co.

59. Bezançon, F., and Weil, M. P.: Proceedings of a Conference on Rheumatic Diseases, Bath, 1928, Bath City Council.
60. Bedford, H. P.: Am. J. Dis. Child. **21**: 139, 1921.
61. Findlay, L.: Rheumatic Infection in Childhood, New York, 1932, William Wood & Company.
62. Ernstene, A. C.: Am. J. M. Sc. **180**: 12, 1930.
63. Peterman, M. G., and Seeger, S. J.: Quoted by Poynton, F. J., and Schlesinger, B., Recent Advances in the Study of Rheumatism, Philadelphia, 1931, P. Blakiston's Son & Co.
64. Boas, E. P., and Schwartz, S. P.: AM. HEART J. **2**: 375, 1927.
65. Poynton, F. J.: Proceedings of a Conference on Rheumatic Diseases, Bath, 1928, Bath City Council.
66. Schlesinger, B.: Quoted by Bach, F., The Rheumatic Diseases, London, 1935, Cassel & Co., Ltd.
67. Allen, G. A.: Quoted in East, C. F. T., and Bain, C. W. C., Recent Advances in Cardiology, Philadelphia, 1929, P. Blakiston's Son & Co.
68. Holtz, E., and Friedman, G.: Am. J. M. Sc. **187**: 359, 1934.
69. Bain, C. W. C., and Hamilton, C. K.: Quoted in Poynton, F. J., and Schlesinger, B., Recent Advances in Rheumatism, Philadelphia, 1931, P. Blakiston's Son & Co.
70. Rothschild, M. A., Sacks, B., and Libman, E.: Quoted in Poynton, F. J., and Schlesinger, B., Recent Advances in Rheumatism, Philadelphia, 1931, P. Blakiston's Son & Co.
71. Reid, W. D., and Kenway, F. L.: Quoted in Poynton, F. J., and Schlesinger, B., Recent Advances in Rheumatism, Philadelphia, 1931, P. Blakiston's Son & Co.
72. Carr, J. G., and Reddick, W. G.: Quoted in Poynton, F. J., and Schlesinger, B., Recent Advances in Rheumatism, Philadelphia, 1931, P. Blakiston's Son & Co.
73. Shapiro: Quoted by Bach, F., Rheumatism: Its Significance in Youth and Middle Age, London, 1930, P. S. King & Son, Ltd.
74. Levy, R. L., and Turner, K. B.: Arch. Int. Med. **43**: 267, 1929.
75. McEachern, D., and Baker, B. M.: Am. J. M. Sc. **183**: 35, 1932.
76. Swift, H. F.: Am. J. M. Sc. **170**: 631, 1925.

# THE PRECIPITATING CAUSES OF CONGESTIVE HEART FAILURE*†

WILLIAM A. SODEMAN, M.D., AND GEORGE E. BURCH, M.D.
NEW ORLEANS, LA.

THE importance of added strain in the precipitation of congestive failure in an overburdened heart has long been recognized. White[1] states that "in a person with heart disease, failure is often precipitated by a relatively trivial circumstance, such as a slight respiratory infection, overeating, or slight overexertion, but usually heart failure is of gradual onset without any particular precipitating factor. In children, acute rheumatic infection is the most frequent immediate cause." Herrmann[2] states that "the establishment of a precipitating factor is of significance in the prognosis and future management of any patient with cardiovascular breakdown." Cowan and Ritchie[3] list the following causes: exercise, pregnancy, hemorrhage, pulmonary infection, emphysema, gastrointestinal disturbances which produce disturbances in nutrition, intoxication, operation, mental shock, starvation in any form, acute exacerbation of chronic renal disease, and surgical shock. This list, of course, is only partial. The number of precipitating causes is limited only by the number of factors capable of causing cardiac or circulatory strain. Donzelot[4] has given a detailed survey of the cardiac and extracardiac conditions responsible for heart failure, but has reported no cases. Davis[5] has considered the traumatic causes.

In a search of the literature we were unable to find a series of consecutive cases of congestive heart failure in which the precipitating cause of the attack had been used to prognosticate the outcome from that attack. Likewise, we were unable to find a consecutive series in which the relative frequency of the precipitating causes had been analyzed. A review of the routine ward histories also indicated that the events leading to the development of congestive failure are not always recorded. These facts prompted us to investigate this problem and necessitated a detailed questioning of each patient regarding the onset of congestive failure.

We have attempted to elicit the precipitating causes in 100 consecutive patients with congestive heart failure entering the Tulane Medical Service of Charity Hospital and the Hutchinson Memorial Clinic during the autumn of 1936. Each patient has been carefully questioned, examined and followed by both of us. All were bedridden. Diagnoses

*Presented before the American Heart Association, Section for the Study of Cardiac Disorders, at Atlantic City, June 8, 1937.

†From the Department of Medicine, School of Medicine, Tulane University of Louisiana, New Orleans, and the Charity Hospital of Louisiana, New Orleans.

were made according to the criteria approved by the American Heart Association, and treatment, including bed rest, digitalization, sedatives, and symptomatic measures, while varying with the patient, was comparable in indications and application.

TABLE I

ETIOLOGY OF HEART DISEASE

| | |
|---|---|
| Hypertension and arteriosclerosis | 30 |
| Arteriosclerosis | 27 |
| Hypertension | 25 |
| Luetic heart disease | 10 |
| Rheumatic heart disease | 7 |
| Congenital | 1 |
| Total | 100 |

The diagnoses as to etiological types are recorded in Table I. Hypertension and arteriosclerosis, separately or in combination, accounted for over 75 per cent of the group; syphilis for 10 per cent; rheumatic fever for 7 per cent, and congenital anomalies for 1 per cent. This distribution is representative of the general incidence of the etiological types of heart disease in our service.

In the majority of cases a precipitating cause was definitely demonstrable. In three individuals, in subsequent attacks, a different precipitating cause was apparent, so that 104 instances were recorded for the 100 individuals. They were distributed as follows: exercise 20; infection (upper respiratory tract 15, acute gastroenteritis 1, acute bacillary dysentery 1, erysipelas 1) 18; pregnancy 5; surgical shock 2; coitus 2; sudden rise in blood pressure 2; psychic trauma 2; hemorrhage 2; heavy meal 1; and alcoholism 1. A gradual onset occurred in 47 patients without demonstrable cause, and an acute onset in two patients, cause not definitely known, but probably a sudden rise in blood pressure. In the 47 patients with gradual onset, 46 were unable with treatment to compensate sufficiently to carry on minimal normal activity. Among those in whom precipitating causes were demonstrable, in 40 compensation was established rapidly and sufficiently under treatment to make the patient able to carry on usual activity, 14 failed to show compensation to that extent, and 3 could not be followed.

## DISCUSSION

Contrary to the views expressed in the literature, in our series over 50 per cent of the patients had a definite precipitating factor leading to the development of congestive failure. Had we been able to elicit a satisfactory history in every case, particularly in those of long standing, the percentage might have been higher. Again, precipitating causes may have been present but not evident to the patient. Even a careful history would fail to elicit them.

The relative frequency of the precipitating factors would doubtless vary in any series with the race, age, and sex of the patients, climatic conditions of the particular area, the season of the year, and any other conditions which vary the incidence of disease and the occupations and habits of the patients. Although these factors may influence the relative frequency of the precipitating causes of heart failure and of heart failure itself, we were unable to demonstrate the influence of any of these factors upon the ability or inability of the patients in our group to reestablish compensation. Such data are of great importance and can be obtained only by the comparison of entire groups similar to this one.

As mentioned previously, a gradual onset of congestive failure occurred in 47 patients without demonstrable precipitating cause. That 46 of these individuals were unable to compensate sufficiently to carry on minimal activity is strikingly evident and points out clearly the value of the determination of the type of onset in prognosis. Such patients usually developed evening edema which became progressively worse for a varying period of time until they were bedridden. It appears that these patients had had no forewarning of the progressive diminution in their cardiac reserve until it was so diminished that even minimal activity exceeded it. However, had such a patient a warning of diminishing cardiac reserve by a precipitating factor before this limit were reached, he probably would have reacted to treatment and would have been able to adjust his activity to meet his existing cardiac reserve. Furthermore, treatment of any correctible etiological factor could have been instituted to prevent further encroachment upon the heart. These statements are borne out by the progress of our cases with a known precipitating cause. In 40 of the 57 instances with a known precipitating cause the patients compensated rapidly with treatment and sufficiently to carry on usual activities. Fourteen failed to compensate to that extent and 3 could not be followed. Four of the 14 patients had syphilitic aortic regurgitation, while in the group with ability to compensate there were none with this condition. It is possible that in the remaining 10 instances the patients were already on the verge of failure when the precipitating cause intervened. Omitting the 4 patients with syphilitic aortic regurgitation, who seem to form a special group, the patients with distinct precipitating causes had a 75 per cent chance of recovering compensation; those without a known precipitating cause over 95 per cent chance of not recovering compensation.

Infection and exercise are the usual precipitating causes emphasized in the literature. In our series these constituted 38 of the 55 instances of known precipitating causes. Even though these factors may be helpful in diagnosis, and later in prognosis, in patients with heart disease, they are always detrimental and should be avoided.

The 5 patients with pregnancy as a precipitating cause deserve special consideration. Three of these developed congestive failure in the third

trimester. They represent the usual type of patient with congestive failure precipitated by the increased strain of pregnancy. All three of these patients reestablished compensation satisfactorily following delivery. The remaining two are representative of a group in which congestive failure occurs post partum. A search of the literature indicates that cardiac decompensation at that time is most unusual in the absence of vascular complications. In our patients congestive failure was absent during pregnancy and developed for the first time in the puerperal period within three weeks following delivery. We see in these patients the remarkable fact that congestive failure occurred for the first time after the release of the usual strain of pregnancy upon the heart. The history, course, and physical findings make up a characteristic picture, but the mechanism by which failure was precipitated is not clearly understood. A series of patients of this type and the possible mechanisms involved are described in detail elsewhere.[6] One of the two patients in the present series died in heart failure. The other is living but has failed to compensate sufficiently to carry on minimal activity.

Two patients with hypertension, followed before the onset of congestive failure, developed decompensation immediately after a sudden rise in blood pressure. The cause of the rise in the pressure could not be determined. No other possible precipitating causes could be elicited at that time. This evidence strongly suggests that the sudden rise in blood pressure precipitated the failure. With a reduction in blood pressure to the former level compensation was reestablished. Two other patients not followed before the development of congestive failure, and without any known precipitating cause, displayed the same picture. These patients are listed in Table II as sudden onset of unknown cause.

TABLE II

PRECIPITATING CAUSES OF CONGESTIVE HEART FAILURE

| CAUSE | INCIDENCE | NUMBER COMPENSATED WITH TREATMENT | NUMBER NOT COMPENSATED WITH TREATMENT |
|---|---|---|---|
| Gradual onset (cause unknown) | 47 | 1 | 46 |
| Infection | 18 | 12 | 6 |
| Exercise | 20 | 14 | 6 |
| Pregnancy | 5 | 3 | 2 |
| Sudden rise in blood pressure | 2 | 2 | 0 |
| Sudden onset (cause unknown) | 2 | 2 | 0 |
| Psychic trauma | 2 | 1 | 1 |
| Hemorrhage | 2 | 1 | 1 |
| Surgical shock | 2 | 1 | 1 |
| Coitus | 2 | 2 | 0 |
| Heavy meal | 1 | 1 | 0 |
| Alcoholism | 1 | 1 | 0 |
| Total | 104 | 41 | 63 |

A sudden rise in blood pressure suggests itself as the precipitating cause in these patients. Since a sudden rise in blood pressure may be asymptomatic, it is possible that it may be active as a precipitating cause with no evidence in the history.

The mechanisms of psychic trauma, hemorrhage, postoperative shock, coitus, overeating, and alcoholism as precipitating causes of congestive failure are self-evident.

The importance of the etiological diagnosis in predicting the outcome in the presence or absence of a precipitating cause was considered. It was found to be a factor in those with syphilitic aortic regurgitation. In these patients the prognosis was poor regardless of the precipitating cause. These observations are in keeping with the usual grave prognosis given such patients when cardiac compensation has once been broken.

It is stated in the literature that active rheumatic carditis is often a precipitating cause of congestive failure in patients with chronic rheumatic endocarditis. In our seven patients signs of active rheumatic fever could not be elicited. Furthermore, three of these patients had a definite precipitating cause unrelated to rheumatic fever. The remaining four had a gradual onset without any demonstrable precipitating cause. It is possible that an unrecognized active carditis may have played a rôle in the development of failure in these patients.

## SUMMARY AND CONCLUSIONS

A study of 100 consecutive cases of congestive heart failure indicates that:

1. In 55 (52.9 per cent) of 104 instances of congestive failure a definite precipitating cause was demonstrable.

2. The reaction to therapy was poor following congestive heart failure with a gradual onset without demonstrable precipitating cause. Over 95 per cent of these patients failed to compensate sufficiently to carry on minimal activity.

3. We were usually able to prognosticate a good response to treatment in patients with a definite precipitating cause provided the cause could be removed. In 75 per cent of these patients removal of the precipitating cause fostered rapid and sufficient recovery of cardiac reserve to permit at least minimal activity.

4. The precipitation of congestive heart failure by a factor putting a strain on the heart acts as a forewarning of the existence of lowered cardiac reserve so that with treatment and adaptation the patient's life may be prolonged. Such a factor, however, is always detrimental to the heart.

5. Following congestive failure patients with syphilitic heart disease with aortic regurgitation showed an inability to compensate regardless of the precipitating cause. The etiological diagnosis otherwise was not found to be significant.

## REFERENCES

1. White, P. D.: Heart Disease, ed. 2, New York, 1937, The Macmillan Company.
2. Herrmann, G. R.: Synopsis of Diseases of the Heart and Arteries, St. Louis, 1936, The C. V. Mosby Company.
3. Cowan, J., and Ritchie, W. T.: Diseases of the Heart, ed. 3, Baltimore, 1935, William Wood and Company.
4. Donzelot, E.: Les Causes de l'insuffisance cardiaque, Le monde medicale 46: 97, 1936.
5. Davis, N. S.: Cardiovascular Disease and Industry, Indust. Med. 3: 83, 1934.
6. Musser, J. H., Turner, R. H., and Sodeman, W. A.: Tr. A. Am. Physicians. (In press.)

# RELATION OF MYOCARDIAL DISEASE TO ABNORMALITIES OF THE VENTRICULAR COMPLEX OF THE ELECTROCARDIOGRAM*†

HAROLD E. B. PARDEE, M.D., AND LEO PRICE, M.D.
NEW YORK, N. Y.

THE finding of an abnormal ventricular complex in the electrocardiogram is commonly used as a basis for the diagnosis of myocardial disease, but discrepancies between the electrocardiographic diagnosis and autopsy findings have occasionally been reported. It seems worth while therefore to review a considerable number of cases with the idea of determining the reliability of electrocardiographic evidence in diagnosing the presence or absence of morphological changes in the ventricular myocardium. Sixty cases have been selected for this study. The records of all autopsies performed at the New York Hospital between Sept. 20, 1930 and July 4, 1932, were reviewed, including cases from both the medical and the surgical services. Those cases were selected for study that had electrocardiographic records made shortly before death and had neither received digitalis nor quinidine recently enough for these to have influenced the record. Only the standard leads were obtained in these cases.

The electrocardiographic record was considered abnormal when those features were discovered in the ventricular waves which have been commonly considered to indicate myocardial disease. These are as follows: duration of QRS exceeding 0.10 seconds; notching or slurring of QRS near the peak of a large wave and in more than one lead of the record; voltage of the QRS group less than 5 mm.; $Q_3$ measuring more than 25 per cent of the largest excursion of QRS excepting in the presence of right axis deviation; R-T or S-T junction occurring more than 1 mm. above or below the P-R level; diphasic, isoelectric or downward T-waves in Leads I or II or in both; significant changes in the voltage or other features of the QRS or T-waves observed in records of the same patient taken a few days from one another.

It is to be emphasized that only when these features were quite definite have they been made the basis of a diagnosis of *abnormal ventricular complex*. Notching and slurring were especially carefully scrutinized and were not considered positive unless evident in two leads and in one of these involving a part of QRS remote from the base line. When the

*From the New York Hospital and the Department of Medicine, Cornell University Medical College.

†Preliminary report presented before the Association of American Physicians, May, 1937.

complex was such as to indicate bundle-branch block it was not also considered under the categories of notched, wide QRS or inverted T, even though these features might have been present.

Auricular fibrillation, auricular flutter, and heart block have been omitted from this list of electrocardiographic abnormalities. This has been done because, though these physiological disturbances often have a basis in structural myocardial disease, yet such changes would be expected in the auricles or in the A-V conduction system and not in the ventricular myocardium, which alone has been subjected to careful pathological study. Premature beats and paroxysmal tachycardia may also arise because of structural myocardial disease but they may so often be neurogenic in origin that it was not considered proper to attempt to correlate them with morphological changes. Our purpose then has been to determine the relation between the normal and abnormal ventricular complex and a morphologically normal or abnormal ventricular myocardium.

The general autopsy findings, the gross appearance of the pericardium and valves, the condition of the coronary vessels, the gross appearance of the heart muscle, and the microscopic appearance of sections from areas suspected of being abnormal were tabulated. Usually two or three sections were available for microscopic study from each heart, sometimes only one.

Pathological changes in the endocardium and aorta were not tabulated unless of evident clinical importance, as they were not considered capable of causing changes in the ventricular complex. The degree of coronary arteriosclerosis has been noted under the categories of slight, moderate, or marked. Although thrombosis of a branch may occur when the appearance of the remainder of the coronary tree is such as to indicate only moderate arteriosclerosis, yet such a case is noted as "marked" because of the degree of the change in the one branch which became thrombosed. When the term atheroma appeared in the original autopsy protocol it was carried over without change to our tables because it was thought best not to change the terminology of the recording pathologist. It is felt that atheroma of the coronaries is but one manifestation of arteriosclerosis of these vessels.

Morphological changes in the myocardium are especially stressed because it is felt that some such definite finding might account for permanent changes in the electrocardiogram. Lesions of the myocardium are considered separately from lesions of the coronary arteries because it is believed that the electrocardiogram can only be influenced by changes in the physiology of the myocardium. It is possible that coronary narrowing may so reduce the blood supply to the muscle fibers as to change the electrical curve without there being any morphological changes in the

fibers. It is impossible, however, to evaluate the degree of coronary narrowing with sufficient exactness to allow a correlation of this such as has been attempted here with morphological myocardial changes. It is also known that toxic influences and inflammation as in diphtheria and rheumatic fever may affect the muscle fibers so as to change the electrical curve. Sometimes toxic influences may produce morphological changes as well, but inflammation of course will always do so.

The ventricular myocardium, including under this term the muscular and fibrous tissue structure, was considered to show structural disease when the following morphological changes were found: (1) inflammatory changes: (a) exudative or proliferative lesions, be they localized or diffuse, such as are found in rheumatic or bacterial infections; (b) fibrosis resulting from acute or chronic inflammatory changes; (2) non-inflammatory changes, such as: (a) replacement fibrosis in areas of atrophied muscle fibers due to coronary narrowing, also scars following infarction due to coronary occlusion; (b) increase of intramuscular fibrous tissue; (c) fatty degeneration; (d) granular degeneration. It will be noted that these changes are demonstrable chiefly on microscopic examination.

Table 1 shows the relation of normal and abnormal ventricular complexes to normal or abnormal autopsy findings in the sixty cases studied.

TABLE 1.—RELATION OF VENTRICULAR COMPLEX AND AUTOPSY FINDINGS

| | Ventricular Myocardium | |
|---|---|---|
| | Diseased | Normal |
| 47 abnormal complexes | 38 (81 per cent) | 9 (19 per cent) |
| 13 normal complexes | 6 (46 per cent) | 7 (54 per cent) |

Of the 47 cases with abnormal ventricular complexes 81 per cent were found to have morphological changes in the ventricular myocardium and 19 per cent had apparently normal myocardium. Of the 13 cases with normal ventricular complexes 46 per cent were found to have morphological changes while 54 per cent had normal myocardiums. There was agreement between the electrocardiographic diagnosis and the autopsy findings in 45 cases, 75 per cent of the whole series, and disagreement in 25 per cent. The agreement was greater when the electrocardiogram was abnormal (81 per cent) than when it was normal (54 per cent).

With a normal electrocardiogram there appears to be about an equal chance for the myocardium to be found normal or diseased. This observation should lead us to be very cautious in interpreting a normal electrocardiogram as an indication of a normal myocardium. In doubtful cases we should take additional records or, if this is not possible, should rely for our diagnosis upon other clinical signs of myocardial disease, such as enlargement of the heart, abnormality of the heart sounds, or abnormal cardiac functional tests.

Of the seven cases with normal electrocardiograms and normal myocardium none had heart disease; one had slight coronary arteriosclerosis; one died of uremia and revealed fibrinous pericarditis with a heart weighing 550 gm.

Table 2 gives the morphological findings in the six cases with normal ventricular complex and an abnormality of the myocardium. These cases merit special attention because a negative diagnosis was made in the presence of myocardial disease. Only one of them had a clinical diagnosis of heart disease, Case 20. None died of heart failure. There were no gross focal lesions in any of these hearts nor any lesion of the muscle fibers. Changes in the interstitial tissue were slight in the first three

TABLE 2.—CASES WITH NORMAL VENTRICULAR COMPLEX—PATHOLOGIC CHANGES ON AUTOPSY.

| Case No. | Age. | Cause of death. | Heart wgt., gm. | Gross appearance. | Microscopic findings in ventricles. |
|---|---|---|---|---|---|
| 9 | 56 | Bronchopneumonia; secondary anemia | 425 | Normal | Slight increase of interstitial fibrous tissue |
| 17 | 51 | Post-thyroidectomy (for Graves' disease), mediastinal hemorrhage and edema of larynx | 350 | Coronaries normal | Slight increase of fibrous tissue |
| 19 | 65 | Carcinoma of bile duct; bronchopneumonia | 350 | Muscle pale; coronaries normal | Few small areas of fibrosis |
| 20 | 19 | Acute septic endocarditis; mitral valve | 300 | Petechiæ; coronaries normal | Polymorphonuclear foci in both ventricles, perivascular distribution, and scattered through interstitial tissue |
| 21 | 59 | Bronchopneumonia and pleurisy | 235 | Coronaries normal | Increased interstitial tissue especially in left ventricle |
| 18 | 79 | Bronchopneumonia | ? | Subendocardial hemorrhages; coronaries—slight atheroma | Increased fibrous tissue in left ventricle |

cases, moderate in the last three. The coronary arteries were normal in all but one case which showed slight coronary arteriosclerosis.

The nine cases of Table 3 showed an abnormal ventricular complex and a normal myocardium. These cases merit special attention because a positive diagnosis of myocardial disease was erroneously made on the basis of the abnormal features of their electrocardiograms. Five of them had a clinical diagnosis of heart disease (Cases 2, 4, 6, 7 and 14) three dying of cardiac insufficiency. Coronary arteriosclerosis was absent in three cases, slight in four, and moderate in two. Their electrocardiograms appear in Figs. 1, 2, and 3.

In seeking an explanation for the appearance of an abnormal electrocardiogram in these cases without myocardial degeneration or fibrosis, it may be noted that Case 7 had a very large heart and shows (Fig. 2*C*) the type of ventricular complex which has been attributed to marked

TABLE 3.—CASES WITH ABNORMAL VENTRICULAR COMPLEX. NO PATHOLOGIC CHANGES IN MYOCARDIUM.

| Case No. | Age. | Electrocardiogram. | | Cause of death. | Cardiac autopsy findings. |
|---|---|---|---|---|---|
| | | *QRS.* | *T.* | | |
| 1 | 64 | Deep *Q*–3; left axis | Normal | Cerebral hemorrhage | 350 gm.; left ventricular hypertrophy slight; coronaries moderate arteriosclerosis; myocardium slight fatty infiltration |
| 2 | 50 | Normal axis; wide | *T*–2 diphasic six months before death; normal four days before death | Lobar pneumonia; coronary arteriosclerosis | 390 gm.; hypertrophy slight; coronaries slight arteriosclerosis; myocardium normal |
| 4 | 42 | *Right bundle branch block | | Heart failure; chronic valvular disease; mitral stenosis and insufficiency | 460 gm.; left ventricle increased thickness; right ventricle dilated; coronary arteriosclerosis slight; myocardium normal |
| 5 | 45 | Normal axis; notched; low voltage | High voltage | Bronchopneumonia, septicemia | 360 gm.; myocardium normal; coronaries negative |
| 6 | 26 | Right axis; wide; notched | †*T*–2 iso-electric | Heart failure, pulmonary embolism; chronic valvular disease; rheumatic aortic mitral and tricuspid endocarditis | 500 gm.; heart hypertrophied and dilated; coronaries negative; myocardium normal; (muscle fibers increased in size on microscopic examination) |
| 7 | 49 | Left axis; wide; notched; slurred | *T*–1 and *T*–2 negative; *R*–*T*–1 depressed; *R*–*T*–2 elevated | Ruptured aneurysm of aorta | 500 gm.; left ventricle hypertrophy marked; aortic insufficiency; coronaries slight arteriosclerosis; myocardium normal |
| 14 | 53 | Right bundle branch block | | Heart failure; pulmonary emphysema | 490 gm.; right ventricle hypertrophied and dilated; left ventricle hypertrophied; coronaries normal; myocardium normal |
| 22 | 39 | Left axis; low voltage | Normal | Syphilis of liver | 250 gm.; coronary arteriosclerosis moderate; myocardium normal |
| 27 | 38 | Left axis; negative | Low voltage | Lobar pneumonia | 550 gm.; coronaries slight arteriosclerosis; right coronary orifice slightly narrowed; luetic aortitis; aortic insufficiency; left ventricular cavity enlarged; myocardium normal |

* Auricular fibrillation.

† Partial heart block.

hypertrophy of the left ventricle.[1] However, Case 27 with aortic insufficiency and a heart much larger than that of Case 7, did not show this special type of ventricular complex (Fig. 3*C*) so that its association with left ventricular hypertrophy is clearly not obligatory. The low voltage

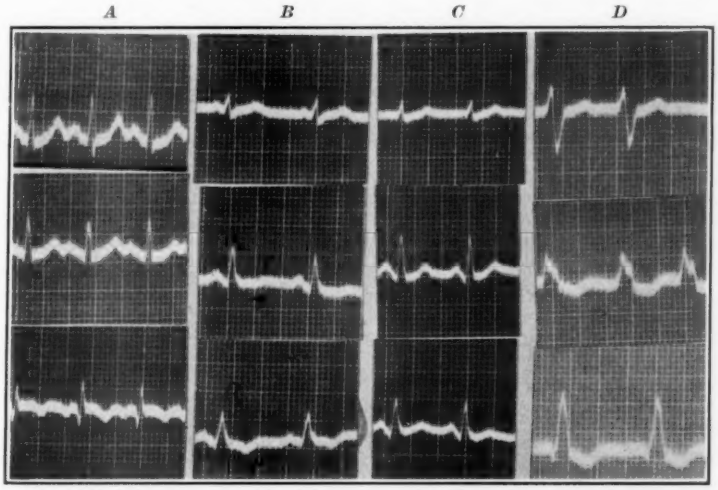


Fig. 1.—*A*. Case 1. *B*. Case 2, six months before death. *C*. Case 2, five days before death. *D*. Case 4.

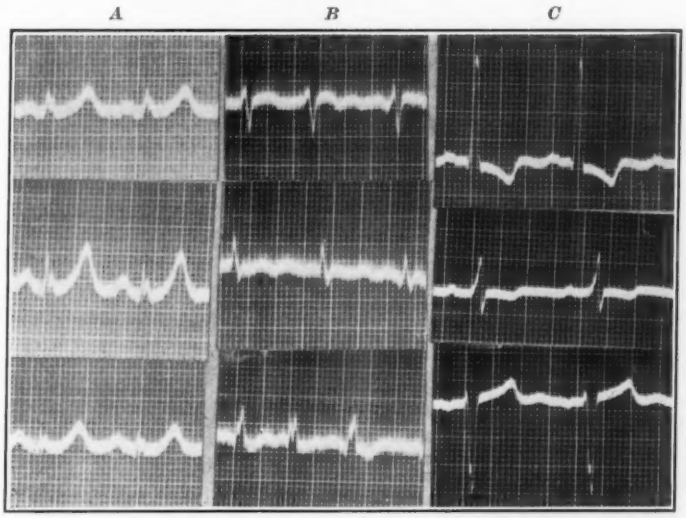


Fig. 2.—*A*. Case 5. *B*. Case 6. *C*. Case 7.

T-wave of Case 27 might be explained as a result of the toxemia of the pneumonia, but the high voltage T of Case 5, also with pneumonia, appears to clash with this idea. The abnormal $Q_3$ of Case 1 might be due to the occurrence of moderate coronary arteriosclerosis and slight fatty infiltration of the myocardium in an adipose individual with a transverse position of the heart.

Case 2 had previously been admitted for an attack thought to be a minor coronary closure, at which time the T-wave was diphasic in Lead II (Fig. 1*B*). The record just before death was normal (Fig. 1*C*). Slight coronary arteriosclerosis and slight hypertrophy were the sole morphological findings. It is possible that the earlier T-wave changes were on a basis of functional muscle disturbance, due to coronary narrowing and a deficient blood flow which had not yet resulted in morphological changes in the muscle fibers or interstitial tissue. It is impossible to deny however that more extensive section cutting might have discovered areas of morphological change.

In Case 22 the hepatic toxemia might explain the low voltage QRS group. No explanation seems possible for the low voltage, notched QRS

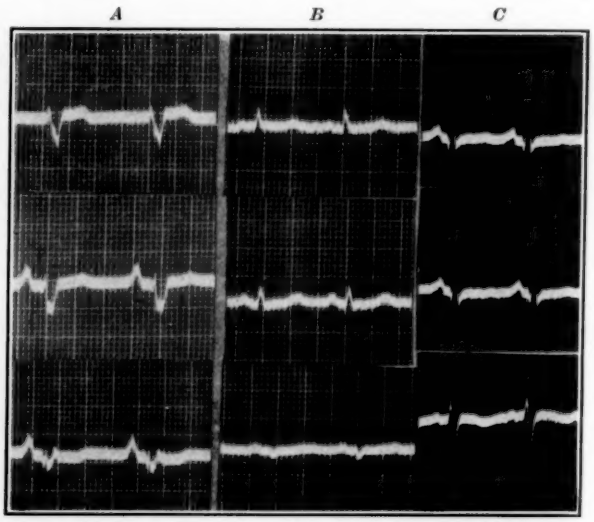


Fig. 3.—*A*. Case 14. *B*. Case 22. *C*. Case 27.

with large T of Case 5 or for the wide notched QRS with isoelectric $T_2$ of Case 6. One can only fall back on the rather weak plea that more extensive microscopic sections from these hearts might have discovered localized changes in morphology. This, however, does seem to be a likely explanation of the failure to find structural changes in Cases 4 and 14 with typical right bundle-branch block[2] for we know that a small lesion in the septum affecting the bundle branch tissue might cause this and a detailed sectioning of the bundle area would be needed to find a small lesion.

Table 4 gives the details of the 38 cases with abnormal ventricular complex and with morphological changes in the myocardium. These have been roughly grouped according to whether the myocardial changes were slight or marked or intermediate. There are ten with slight changes, 3 of these with a clinical diagnosis of heart disease, 14 with moderate

changes, with six cases of clinical heart disease, and 14 with marked changes, 10 with clinical heart disease.

Reviewing the electrocardiographic features of the 53 cases of Tables 2, 3, and 4, one fails to find a close relationship between the degree of the pathological changes and the character of the electrocardiographic abnormality. For example, Case 21 of Table 2 had increased interstitial tissue especially in the left ventricle, and gave a normal electrocardiogram, while Case 24 of Table 4 which had slight fibrosis throughout both ventricles and Case 18 of Table 4, which had acute purulent myocarditis with edema and polymorphonuclear cells in the stroma, had an electrocardiogram with notching and slurring of the QRS group. Case 24 had less evidence of disease than Case 21 whose electrocardiogram was normal. Case 18 had more evidence of disease than Case 24, yet the electrocardiographic changes were the same. Note also Cases 26 and 43 of Table 4, each of which had an inverted $T_1$ of the coronary type. Case 26 showed a mild fibrosis of the myocardium with a few areas of lymphocytic infiltration and few areas of slight edema. Case 43 showed cicatricial scars of the myocardium, roughened pericardium and, on microscopic examination, marked fibrosis. Moreover, Case 30 with only small areas of fibrosis in the myocardium, showed the electrocardiogram of left bundle-branch block.

There were, however, some noteworthy associations of electrocardiographic features with pathological pictures. There were ten cases with marked coronary and acute degenerative myocardial changes. Six of these (Cases 25, 33, 44, 45, 47, and 50) gave electrocardiograms with abnormal elevation or depression of the S-T interval. Infarcts were not always found in these hearts but it is possible that in those without infarcts the marked degenerative myocardial lesions present would affect the electrical curve as does an infarct. Of the four other cases with degenerative myocardial changes (Cases 35, 40, 54, and 61) one gave the electrocardiogram of right bundle-branch block (Case 40) and the other three showed the coronary T-wave commonly associated with a healing coronary lesion. It is of interest to find that all ten hearts with marked myocardial changes due to coronary arteriosclerosis were associated with abnormal electrocardiograms, and all except the one with bundle-branch block showed the T-wave changes commonly recognized as associated with some phase of acute myocardial degeneration.

Of the 5 cases with a T-wave of the coronary type, three (35, 54, and 61, Table 4) showed coronary thrombosis or areas of necrotic myocardium. One case (43, Table 4) showed a roughening of the pericardium with fibrin formation which might have been the cause of the T-wave peculiarity,[5] while the other patient (26, Table 4), who died of uremia, failed to show any focal lesion and only slight coronary and myocardial changes. The predominance of focal myocardial lesions

TABLE 4.—CASES WITH ABNORMAL VENTRICULAR COMPLEX AND MYOCARDIAL DISEASE.

| Case No. | Age. | Electrocardiogram. | | Cause of death. | Gross appearance. | Microscopic of myocardium. |
|---|---|---|---|---|---|---|
| | | *QRS.* | *T.* | | | |
| | | | | | (*Slight changes*) | |
| 15 | 62 | L. axis | *T*–1 inv. | Arteriosclerotic heart disease with failure | 680 gm. enlarged; pericardium normal; coronaries show patches of atheroma | Some increase in size of fibers. Increase of interstitial fibrous tissue throughout |
| 24 | 69 | L. axis; notched and slurred | Normal | Lobar pneumonia | 450 gm. myocardium neg.; pericardium inflamed surface; no fluid; coronaries tortuous with patches of atheroma | Slight fibrosis throughout both ventricles |
| 26 | 38 | Axis normal; *QRS* neg. | *T*–1 inv.; coronary type | Uremia | Not enlarged; myocardium neg.; pericardium normal; coronaries show slight atheroma | Mild fibrosis; few areas of leukocytic infiltration; few areas slight edema |
| 29 | 60 | Axis normal; low voltage | *T*–2 diphasic; low voltage | Lobar pneumonia | 380 gm. myocardium normal; pericardium normal; coronaries slight atheroma | No fibrosis; few areas with lymphocytes and plasma cell infiltration |
| 30 | 33 | Left bundle branch block | | Carcinoma of stomach | 350 gm. myocardium normal; pericardium normal; coronaries normal | Small areas of fibrosis |
| 32 | 72 | Axis normal; low voltage | Low voltage | Purulent bronchopneumonia | Myocardium normal; pericardium normal; coronaries normal | Granular degeneration |
| 42 | 53 | L. axis; notched and slurred | Normal | Bronchopneumonia | 500 gm. myocardium shows greyish areas; pericardium normal; coronaries atheromatous | Some fibrosis |
| 51 | 52 | *L. axis; low voltage | *T*–1 and *T*–2 inv. | Mitral stenosis; cardiac failure | 445 gm. hypertrophy of right ventricle; pale fibrotic patches in myocardium; pericardium normal; coronaries neg. | Slight fibrosis left ventricle |
| 56 | 44 | * L. axis | *T*–1 and *T*–2 inv. | Mitral stenosis; heart failure | 625 gm. dilated and hypertrophied; pericardium neg.; coronaries some atheroma; no narrowing | Very slight fibrosis |
| 57 | 63 | L. axis; wide, notched and slurred | *T*–1 inv. | Acute cholecystitis | 275 gm. myocardium normal; pericardium neg.; coronaries few small atheromatous patches | Slight amount of fibrosis |
| | | | | | (*Moderate changes*) | |
| 3 | 43 | L. axis | Low voltage | Mediastinal tumor; empyema | Heart involved in tumorous mass. Pericardial adhesions; coronaries normal | Slight increase in interstitial tissue |
| 8 | 60 | L. axis; low voltage; notched and slurred | *T*–1 iso-electric | Lobar pneumonia | 800 gm. much enlarged; pericardium normal; coronaries normal | Extreme fibrosis |
| 13 | 61 | †L. axis; wide; notched and slurred | Normal | Arteriosclerotic heart disease; heart failure | 760 gm. enlarged; myocardium pale; pericardium normal; coronaries—thickened walls; right coronary orifice 1 mm. in diameter | Many large muscle fibers; scattered patches of fibrosis |

| | | | | | | |
|---|---|---|---|---|---|---|
| 18 | 29 | R. axis; notched and slurred | Norma | Mitral stenosis and insufficiency; acute endocarditis; heart failure | Heart enlarged; myocardium pale; pericardium normal; coronaries normal | Acute purulent myocarditis; edema; polys in stroma |
| 23 | 72 | L. axis | *T*–2 iso-electric | Subacute bacterial endocarditis | 450 gm. myocardium neg.; pericardium complete fibrous adhesions; small amount of slightly cloudy fluid; coronaries atheromatous | Fragmentation of muscle fibers; slight fibrous infiltration beneath pericardium |
| 28 | 45 | L. axis | Low voltage | Cerebral hemorrhage | 510 gm. hypertrophied; dilated; pericardium normal; coronaries moderate atheroma | Moderate fibrosis both ventricles with small areas where muscle bundles are separated by bands of loosely organized fibrous tissue |
| 39 | 17 | R. axis; notched and slurred | Normal | Mitral stenosis and aortic insufficiency; heart failure | 425 gm. enlarged; myocardium and pericardium neg.; coronaries neg. | Small areas subpericardial fatty degeneration. Slight increase perivascular fibrous tissue; few foci, leukocytes and monocytes; occasional small areas intramuscular fibrous tissue |
| 41 | 70 | L. axis; wide | *T*–1 inv. | General arteriosclerosis; myocardial fibrosis; heart failure | 400 gm. scarred left ventricular wall; pericardium neg.; coronaries calcified and narrowed | Scattered large fibrous scars |
| 49 | 55 | L. axis; wide | *T*–1 inv. | Aortic stenosis: paroxysmal tachycardia; heart failure | 550 gm. hypertrophied; dilated; few pale, fibrous patches; pericardium normal; coronaries few patches atheroma | Hypertrophied muscle fibers; patches of fibrosis |
| 52 | 45 | L. axis; wide; notched and slurred | Normal | Bronchopneumonia | 750 gm. hypertrophy; dilated; areas of fibrosis; suppurative pericarditis; coronary sclerosis | Increase of fibrous tissue; polys and mononuclear infiltration |
| 53 | 12 | Axis normal; low voltage | *T*–2 inv. | Streptococcus septicemia | 225 gm. dilated; greyish-white areas; pericardial normal; coronaries normal | Vessels show intimal proliferation; some vessels occluded; acute myocardial degeneration |
| 54 | 55 | L. axis; wide | *T*–1 inv.; coronary type | Pulmonary abscess; actinomycosis | 525 gm. dilated; hypertrophied; pericardium normal; coronaries show marked atheroma; clot in lumen of left descending coronary | Few fibrotic areas |
| 55 | 78 | L. axis; wide; notched and slurred | *T*–1 and 2 inv. | Perineal abscess | 400 gm. greyish areas in myocardium; pericardium fibrous adhesion between visceral and parietal layers; coronary sclerosis | Fibrosis and hypertrophy of muscle fibers |
| 60 | 82 | *Right bundle branch block | | Bronchopneumonia | 850 gm. dilated; hypertrophied; areas of fibrosis; pericardium normal; coronaries sclerotic | Considerable scattered patchy fibrosis |
| 61 | 55 | Normal axis | *T*–1 and 2 inv.; coronary type | Uremia | (*Marked changes*) 550 gm. dilated; hypertrophied; fibrosis involving posterior papillary muscle; coronaries sclerotic; pericardium neg. | Areas of focal necrosis and cellular infiltration; areas of fibrous replacement |
| 25 | 63 | Axis normal | *T*–2, *T*–3 diphasic; *ST*–2 elevated | Coronary thrombosis | 575 gm. myocardium left ventricle, apex thin and shows grey streaks; pericardium small, amount slightly cloudy fluid; coronaries atheromatous; thrombosis right coronary | Fibrosis; leukocytic infiltration, fibrous tissue apex left ventricle |

* Auricular fibrillation.

† Partial heart block.

TABLE 4.—CASES WITH ABNORMAL VENTRICULAR COMPLEX AND MYOCARDIAL DISEASE.—(*Continued.*)

| Case No. | Age. | Electrocardiogram. | | Cause of death. | Gross appearance. | Microscopic of myocardium. |
|---|---|---|---|---|---|---|
| | | *QRS.* | *T.* | | | |
| | | | | | (*Marked changes—Cont.*) | |
| 33 | 40 | L. axis; wide; notched and slurred | *T*–1 iso-electric; low voltage; *ST*–1 elevated | Myocardial infarct | 720 gm. lower part left ventricle thin and fibrosed; pericardial surface reddened; coronaries thickened and narrowed; occlusion lower part of anterior descending branch left coronary | Areas of necrosis of muscle cells with fibroblasts and leukocytes |
| 34 | 42 | L. axis; wide | *T*–1 and *T*–2 inv. | Arteriosclerotic heart disease; heart failure | 525 gm. myocardium neg.; subpericardial hemorrhage anterior surface; coronaries sclerotic and calcified | Fibrosis marked in left ventricle |
| 35 | 59 | L. axis; large *Q*–3 | *T*–1 and *T*–2 inv.; coronary *T*–2 | Myocardial infarct | 430 gm. dilated; apex of left ventricle infarcted; pericardium neg.; coronaries calcified and narrowed | Fibrosis with area of necrosis |
| 36 | 63 | *Axis normal; wide | *T*–1 iso-electric; *T*–2 neg. | Miliary tuberculosis of the lung; myocardial fibrosis; cardiac insufficiency | 600 gm. myocardium thickened, pale and scarred. Pericardium 100 cc. fluid; coronaries sclerosed and tortuous | Marked diffuse fibrosis |
| 38 | 76 | L. axis | *T*–1 inv.; low voltage | Volvulus | 425 gm. fibrotic areas at apex. Pericardial adhesions and hydropericardium; coronaries marked calcification; left circumflex obliterated | Extreme fibrosis |
| 40 | 53 | Right bundle branch block | | Coronary arteriosclerosis; heart failure | 525 gm. myocardium shows small greyish areas; pericardium neg.; coronaries show atheroma with marked narrowing descending branch of left coronary | Subendocardial round cell infiltration; necrotic muscle cells, areas of fibrosis |
| 43 | 55 | L. axis | *T*–1 inv.; coronary type | Uremia | 425 gm. myocardium shows cicatricial scars; pericardium roughened surfaces; layer of fibrin; slight increase of fluid; coronaries atheromatous and calcified | Marked fibrosis |
| 44 | 52 | Right bundle branch block coronary *T*–1 and *T*–2 | | Myocardial infarct | 505 gm. hypertrophy and dilatation; infarct anterior wall left ventricle; pericardial adhesions; coronary sclerosis marked; thrombosis anterior descending branch left coronary | Marked fibrosis, area of muscle necrosis |
| 45 | 82 | Left bundle branch block *ST*–1 inv.; *ST*–2 and 3 upward | | Arteriosclerotic heart disease; coronary occlusion | 550 gm. old infarct at apex; several fibrotic areas; pericardium normal; coronaries sclerotic; much narrowed | Marked fibrosis, pale muscle fibers |
| 46 | 48 | Axis normal; wide; notched and slurred; large *Q*–3 | *T*–1 iso-electric; low voltage | Septicemia; bronchopneumonia | 325 gm. many areas of fibrosis; pericardium normal; coronaries sclerotic, narrowed | Fibrosis both ventricles |
| 47 | 69 | Axis normal; *QRS* low voltage | *T*–1 inv.; *ST*–1 upward; *ST*–3 inv. | Coronary thrombosis | Enlarged; greyish areas at apex; pericardium normal; coronary sclerosis marked; clot in left coronary | Considerable interstitial fibrosis |
| 50 | 45 | †R. axis | *T*–1 inv.; *ST*–2 and *ST*–3 elevated | Coronary thrombosis | 575 gm. dense fibrosis in left ventricle posteriorly; hemorrhagic area posterior margin right ventricle; pericardial adhesions apex left ventricle; increased fluid; occlusion posterior and anterior descending branches left coronary | Old fibrosis; area infarction |

* Auricular fibrillation.

† Partial heart block.

in these five cases is an important confirmation of the frequent association of this coronary T-wave with the less acute phases of focal myocardial lesions due to coronary narrowing or occlusion. The other two cases serve to emphasize the fact previously demonstrated, that this is not a constant association and may be the result of a different type of myocardial disease.

It is difficult to consider the anatomical basis of the individual abnormal features of the electrocardiogram because these rarely occurred alone in this series. Certain cases, however, showed only a single abnormality of the curve. The one case whose record showed a large $Q_3$ as the sole abnormality (Case 1, Table 3), was found to have a transverse heart, moderate coronary arteriosclerosis, slight fatty infiltration of the myocardium but no degeneration or fibrous changes. There were six cases whose records showed a QRS group significantly notched and slurred with normal T-waves. None of these had a normal myocardium. Two showed slight and four, moderate, diffuse myocardial changes. Two with right axis deviation of QRS (18 and 39, Table 4), had mitral stenosis and moderate diffuse myocardial changes. Two with left axis deviation (24 and 42, Table 4) had atheromatous coronaries and slight diffuse myocardial fibrosis. Two others with left axis deviation (13 and 52, Table 4), and with an increased duration of QRS as well as notching, showed very large hearts (750 gm.), coronary arteriosclerosis and moderate diffuse myocardial changes. That these two very large hearts were the only ones of the six with notched QRS to show abnormal duration as well, is in favor of Lewis' suggestion that abnormal duration of QRS may be due to a considerable increase in thickness of the left ventricular muscle[3] and against Wilson's contention that abnormal duration is usually due to an intraventricular conduction defect.[4]

A further study of the relation of heart size and QRS duration in this series fails to give unqualified support to either theory of its causation. Considering the QRS duration in all records with left axis deviation, excluding those diagnosed as bundle-branch block, it is found that the average heart weight of the 15 with a normal duration was 485 gm. while the average heart weight of the 11 with increased duration was 560 gm. This suggests a direct relation between heart size and QRS duration but there are two very large hearts (case 15, 680 gm., and case 8, 800 gm.) with a normal duration of QRS and one very small one (case 57, 275 gm.) with increased duration. Heart size evidently need not cause QRS prolongation and cannot be its sole cause. One must, of course, consider the possibility of a disproportionate thickening of the left ventricle which might prolong the spreading of the contraction more than it would contribute to an increase in heart size.

Low voltage of QRS was the sole abnormal feature of the curve in one case (22, Table 3) dying of liver toxemia, and in one other case (5, Table 3) it was complicated by a high voltage T-wave in a patient with bronchopneumonia. Neither of these hearts showed morphological myocardial changes, though in the first one there was moderate coronary arteriosclerosis. In all eight hearts with only QRS changes in the electrocardiogram the myocardial changes were negative, slight, or moderate. No instance of marked changes occurred.

When the T-wave was inverted, isoelectric or diphasic in Lead I (7 cases), in Leads II and III alone (6 cases), or in Leads I and II together (10 cases), there was usually some other abnormal feature in the curve. In each of these groups the degree and the character of the pathological changes were so varied that it would be impossible to say that there was a predominant association.

The bundle-branch block cases are interesting as to the varied extent of the pathological changes discovered, for it is found that of five with right bundle-branch block two did not reveal any morphological myocardial changes except hypertrophy, one showed moderate changes, and two marked changes. Of the two cases with left bundle-branch block, one showed slight changes and one marked.

There were only six cases of rheumatic valvular disease. One of these had a normal electrocardiogram (Case 20, Table 2), and one with right bundle-branch block had a negative myocardium (Case 4, Table 3, and Fig. 1). The other four had varied myocardial and electrocardiographic abnormalities.

There were only six cases with slight coronary arteriosclerosis uncomplicated by any other condition which might have affected the electrocardiogram. Two of these had a normal myocardium and normal electrocardiogram though one had shown a diphasic $T_2$ six months before death (Case 2, Table 3, and Fig. 1). One had a normal electrocardiogram with slight increase of fibrous tissue in the left ventricle (Case 48, Table 2). The other three showed various types of myocardial and electrocardiographic abnormality. These cases are too few of either rheumatic or slight coronary arteriosclerotic disease to allow any conclusion to be drawn except that either may exist with or without myocardial changes and with or without electrocardiographic abnormality. In either etiological group those cases with definite myocardial changes are much more likely to have electrocardiographic abnormality than are those with normal myocardium.

Three patients died of uremia, 26, 61, and 43. They showed various degrees of coronary arteriosclerosis and myocardial disease, and case 26 only slight changes. It is significant that all three showed $T_1$ inversion with the "coronary type" of curve. This association has been also noted by others.

A review of the literature revealed but few comparable observations. Either the electrocardiographic criteria were not clearly stated or the autopsy reports did not include a statement of microscopic findings, or only cases with abnormal electrocardiograms had been considered.

Nathanson[6] published 7 suitable case reports (his series numbers 1, 2, 3, 5, 6, 7, 9), but only reported upon cases showing an abnormal electrocardiogram. In each heart he found marked coronary and myocardial disease.

Willius and Brown[7] published 20 suitable case reports (cases 2, 3, 5-8, 10, 11, 12, 14-19, 21-25) 9 with normal and 11 with abnormal inversion of T ($T_1$ or $T_2$). They did not consider any other abnormality of the ventricular waves, except T-wave inversion. Four cases showed normal T-waves and normal muscle, 9 showed abnormal T-waves and abnormal muscle, 5 showed normal T-waves and abnormal muscle, 2 showed abnormal T-waves and normal muscle. This represents agreement in 65 per cent, disagreement in 35 per cent, very like the agreement in 75 per cent and disagreement in 25 per cent of the present group.

Saphir, Priest, Hamburger, and Katz[8] studied a series of cases found at autopsy to have "advanced coronary arteriosclerosis"; 19 of these had suitable autopsy reports and electrocardiograms and all showed abnormal records and definite myocardial changes.

Rykert and Hepburn[1] studied 20 cases showing a special type of abnormality of the electrocardiogram seen in Fig. 2*C* which they believed due to marked left ventricular preponderance or hypertrophy. All but four of their cases showed definite morphological myocardial changes of various types but these four showed only hypertrophy of the individual muscle fibers.

The only series of cases really comparable with the present one are those of Markel and Pardee[9] with 10 cases and Master and Pardee[10] with 11 cases, two of which are unsatisfactory because of digitalis administration having affected the T-waves. The 19 suitable cases of these two series were studied in much the same manner as the present group and included 3 with normal electrocardiograms and normal myocardium, 16 with abnormal electrocardiograms and abnormal myocardium, there being no such lack of agreement as was found in the cases of Tables 2 and 3 of the present group. These 19 cases showed on the average more marked pathological changes than the present series, probably because they were selected solely from the medical wards and did not include some of the less important cardiac lesions found in the present group selected from the autopsy service of the entire hospital.

## DISCUSSION

From these observations it seems that the only electrocardiographic abnormality which we can constantly associate with severe morphological

changes is an abnormal deviation of the S-T interval. Further, when the T-wave is not inverted, even though there be abnormalities of the QRS group or a low voltage of T, we should expect to find mild rather than severe lesions.

Case 7, Table 3, and four cases reported by Rykert and Hepburn, suggest that marked left ventricular hypertrophy without other morphological changes may at times cause a characteristic deformity of QRS, and T and the S-T interval.

The finding of a normal record does not exclude the presence of slight or moderate interstitial fibrosis or a subacute inflammatory reaction in the interstitial tissue, for such things were found in the cases of Table 2. On the other hand, an abnormal record, even of right bundle-branch block does not with certainty indicate the presence of coronary disease or of morphological myocardial changes of any considerable extent. Slight coronary arteriosclerosis was sometimes associated with an abnormal electrocardiogram, more usually so when there were also morphological myocardial changes. Coronary arteriosclerosis, if more than slight, was always associated with an abnormal electrocardiogram. Rheumatic valvular disease was also more likely to be found associated with an abnormal electrocardiogram when myocardial changes were present.

The closest relation between the myocardial changes and the electrocardiogram was found in the group with marked coronary disease. All of these hearts gave electrocardiograms with definite abnormalities and when there were large areas of degenerated myocardium the T-wave changes commonly associated with coronary disease were always present—either the R-T deviation associated with infarction or the coronary T-wave associated with a healed or healing lesion.

The lack of correlation between the morphological myocardial changes and the electrical curve is explainable on several grounds. Since the electrical curve is produced by the action of the muscle fibers, a deficient coronary flow may conceivably cause changes in function without for a time, changes in structure taking place (Case 2, Table III, and Fig. 1, *B* and *C*). Moreover, it seems possible that similar functional changes in the muscle may arise with different structural backgrounds. This is apparent in the cases of Tables III and IV, where similar ventricular complexes are seen to arise with a quite different myocardial picture. Some of the instances of failure to find myocardial changes (Table III) may be due to the limited amount of the myocardium examined microscopically. This is especially so in the cases with right bundle-branch block, for here a relatively small lesion involving the bundle branch would not attract attention on gross inspection, and sections of the affected area would not be made.

It is felt that further progress in correlation of electrocardiograms and autopsy findings will only be possible when the myocardium is examined

in more numerous areas and particularly in relation to the position of the heart in the chest. Many of the anatomical descriptions in these autopsy protocols referred to the heart in such a way that it was not possible to decide whether the lesion was on the anterior or diaphragmatic or posterior or lateral walls of the heart. This geographical distribution of lesions is very important in its bearing on electrocardiographic diagnosis and therefore warrants much more attention than it has previously received.

## SUMMARY

Sixty cases have been studied in attempting to determine a relation between the character of the ventricular complex of the electrocardiogram and the pathological findings in the ventricular myocardium.

Of 13 cases with a normal ventricular complex, a normal myocardium was found in 7. In the other six there were slight morphological changes.

Of 47 cases with abnormal ventricular complexes a normal myocardium was found in 9 (19 per cent). The abnormal features of the electrocardiograms in these 9 cases were similar to those found in other cases which revealed slight or moderate pathological changes in the myocardium. In the other 81 per cent of cases with abnormal ventricular complexes there were definite myocardial changes. When the electrocardiographic abnormality involved only the QRS group, the T-wave being normal, there were found only slight or moderate myocardial changes.

Although there was, in general, an association of increased duration of QRS with cardiac enlargement, yet there were notable exceptions.

When the T-wave was abnormal, with or without QRS abnormality, there was a great range in the extent and the degree of the myocardial changes discovered. A frequent but not constant association was seen between the coronary T-wave and focal myocardial lesions. There was a constant association between an elevated or depressed S-T interval and the finding of areas of acute myocardial degeneration, though not always with areas of infarction. The ventricular complex attributed to marked left ventricular hypertrophy affords an exception to this statement regarding the S-T interval.

Right bundle-branch block occurred twice without morphological myocardial changes being discovered and three times with such changes. Left bundle-branch block occurred twice, each time associated with myocardial changes.

A review of the literature showed a few comparable studies, all of which were in general agreement with these findings.

The authors wish to acknowledge their indebtedness to Dr. Robert A. Moore for help in reviewing many of the microscopic sections.

REFERENCES

1. Rykert, H. E., and Hepburn, J.: Electrocardiographic Abnormalities Characteristic of Certain Cases of Arterial Hypertension, AM. HEART J. **10**: 942, 1935.
2. Wilson, F. N., Macleod, A. G., and Barker, P. S.: The Order of Ventricular Excitation in Human Bundle-Branch Block, AM. HEART J. **1**: 305, 1932.
3. Lewis, T.: The Spread of the Excitatory Process in the Vertebrate Heart, Phil. Tr., Lond., B. **207**: 221, 1916.
4. Wilson, F. N., and Hermann, G. R.: The Relation of the QRS Interval to Ventricular Weight, Heart **15**: 135, 1930.
5. Scott, R. W., Feil, H. S., and Katz, L. N.: The Electrocardiogram in Pericardial Effusion, AM. HEART J. **5**: 68, 1929.
   Porte, D., and Pardee, H. E. B.: The Occurrence of the Coronary T-Wave in Rheumatic Pericarditis, AM. HEART J. **4**: 584, 1929.
6. Nathanson, M. H.: The Electrocardiogram in Coronary Disease, AM. HEART J. **5**: 257, 1930.
7. Willius, F. A., and Brown, G. E.: Coronary Sclerosis: An Analysis of Eighty-Six Necropsies, Am. J. M. Sc. **168**: 165, 1924.
8. Saphir, O., Priest, W. S., Hamburger, W. W., and Katz, L. N.: Coronary Arteriosclerosis, Coronary Thrombosis and the Resulting Myocardial Changes, AM. HEART J. **10**: 567 and 762, 1935.
9. Markel, A. G., and Pardee, H. E. B.: The Correlation of Electrocardiographic and Necropsy Findings, Am. J. M. Sc. **176**: 479, 1928.
10. Master, A. W., and Pardee, H. E. B.: The Effect of Heart Muscle Disease on the Electrocardiogram, Arch. Int. Med. **37**: 42, 1926.
    Preliminary report J. A. M. A. **80**: 98, 1923.

# OBSERVATIONS ON THE CARDIO-ACCELERATOR REFLEX FROM STIMULATION OF THE SKIN TEMPERATURE RECEPTORS*†

SIMON BENSON, PH.D.
CHICAGO, ILL.

## I. THE INFLUENCE OF AGE UPON THE EFFECT OF SKIN TEMPERATURE STIMULATION ON THE HEART RATE

AS INDICATED in our previous report,[2] the heart rate appears to be influenced to a much greater degree by the skin temperature than by the body temperature itself. That is, by lowering or raising merely the skin temperature, the heart rate may be decreased or increased, quite independently of any changes in the body temperature.

Further studies now seem to indicate that the efficiency of this reflex action between the skin sense organs and the heart rate tends to vary inversely as the age of the individual. That is, the sensitivity—the degree and promptness—with which the heart reacts to the skin temperature changes, becomes less pronounced with age. We have aimed to illustrate this modifying influence of age in Charts 1 to 6.

The media employed in changing the skin temperature were water, air, and radiant heat. For the water applications we used a Crane continuous flow tub in which the inlet is constructed to mix the incoming flow so thoroughly as to insure a temperature uniformity of within one degree throughout the tub. The assurance of such uniform temperature throughout the tub is of high importance in such tests as these discussed here, since we have found that variations in skin temperature over such a fractional body area as the foot and lower leg, exercise a definite influence upon the heart rate.

Fig. 1 shows our set-up as used with the water bath. As mentioned in our previous report[2] we obtained by this method a continuous mechanical recording of the bath (skin) and body temperatures as well as the pulse (heart) rate.

For the hot air-radiant heat applications, we used a Burdick horizontal type cabinet, slightly modified for our experiments. The temperature changes and the heart rate were obtained by the same mechanical

*From the Department of Physiology, University of Chicago.

†These studies were made possible primarily through the efforts and support of Professor A. J. Carlson, chairman of the department of physiology, and also through the cooperation of Athletic Director T. N. Metcalf in whose department the work was carried out. Our thanks also go to Dr. E. B. Bay, associate Dean of Rush Medical College, for helpful criticism of the manuscript.

The following companies furnished most of the apparatus necessary:

Consolidated Ashcroft Hancock Co., Inc.; The Brown Instrument Company; The Burdick Corporation; The Crane Company; The Powers Regulator Company.

methods as described above for the water bath, except that the air temperature of the cabinet was read by means of a mercury thermometer placed about six or eight inches from the body. The initial temperature of the cabinet was about 80° F. for each experiment, and the thermometer was read at five-minute intervals, or oftener, throughout the experiment.

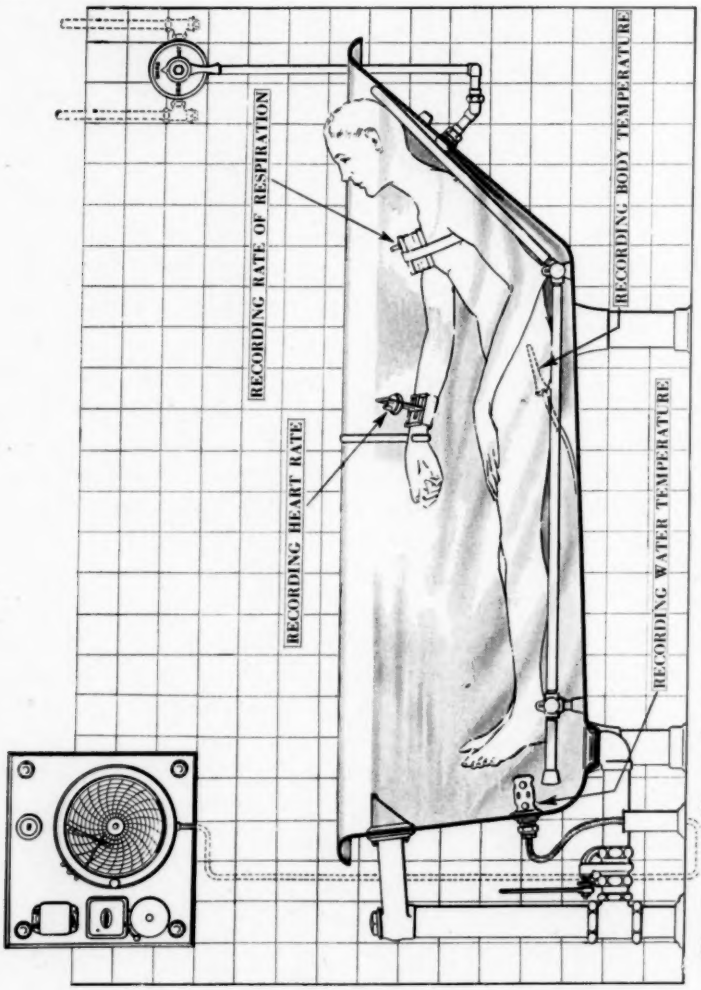


Fig. 1.—Scientific equipment and methods used with water in the determination of the relative influence of external and body temperature upon the heart. (By courtesy of the Crane Company, Chicago, Ill.)

In view of the relationships indicated in this paper between the bath (skin) temperatures and the heart rate, it should be emphasized here that while the temperature of the water is transmitted uniformly to all parts of the skin submerged, the temperature of the hot air and the radiant energy are not transmitted with equal uniformity to all parts of the skin enclosed in the cabinet. The reason being, of course, that the part of the body (usually the back) resting on the floor of the horizontal cabinet cannot be directly affected by the radiant heat emitted from the

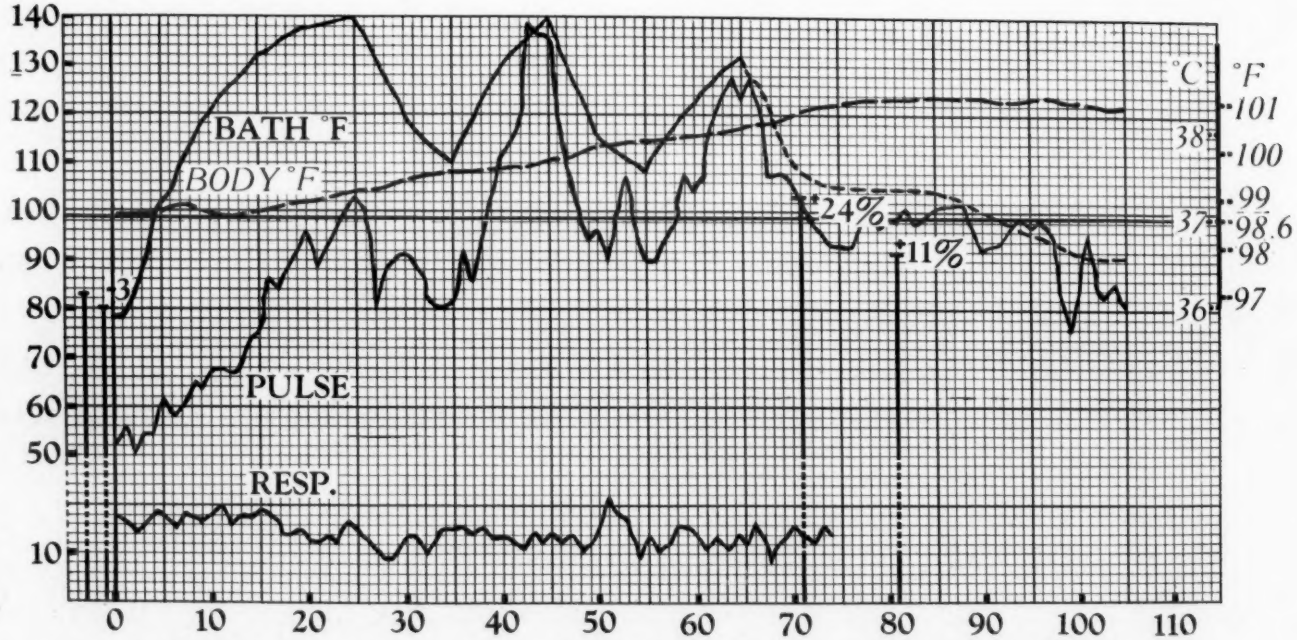


Chart. 1.—Subject F. P., aged twenty years. The numbers across the bottom of the chart denote time in minutes.

Charts aiming to show the influence of age upon the skin (temperature) -heart (rate) relationship.

Key to the Charts: Body temperature, designated by the long broken line, is to be read by the scale on the right; bath (cabinet) temperature, pulse, respiration, and metabolism by the scale on the left. Metabolic rates are expressed on the first four charts by perpendicular lines as follows: The first perpendicular line (Chart 1) close to the left-hand margin, represents the individual's basal metabolism rate (calculated) and is seen to equal about 83; the next perpendicular line, just to the right of the first, represents the individual's observed metabolic rate just before the experiment, and equals about 80, or about 3 per cent less than the calculated basal metabolic rate. This is indicated at the top of the line by a -3. Metabolic rates of +24 per cent and +11 per cent are similarly indicated at the 71st and 81st minutes, after the cabinet heat was shut off. The graph designating the bath (cabinet) temperature changes from a solid to a broken line at the 65th minute, at which time the cabinet heat was shut off. The subject, however, remained in the cabinet undisturbed (except for the metabolic tests) until the 105th minute. For detailed analysis see text.*

*We gratefully acknowledge the assistance of the Crane Company, whose commercial artist made the final copy of these charts.

top and sides of the cabinet, nor very effectively so by the hot air itself. This fact, no doubt serves to explain in part, the difference in effects upon the heart by the water bath and the radiant heat-hot air bath.

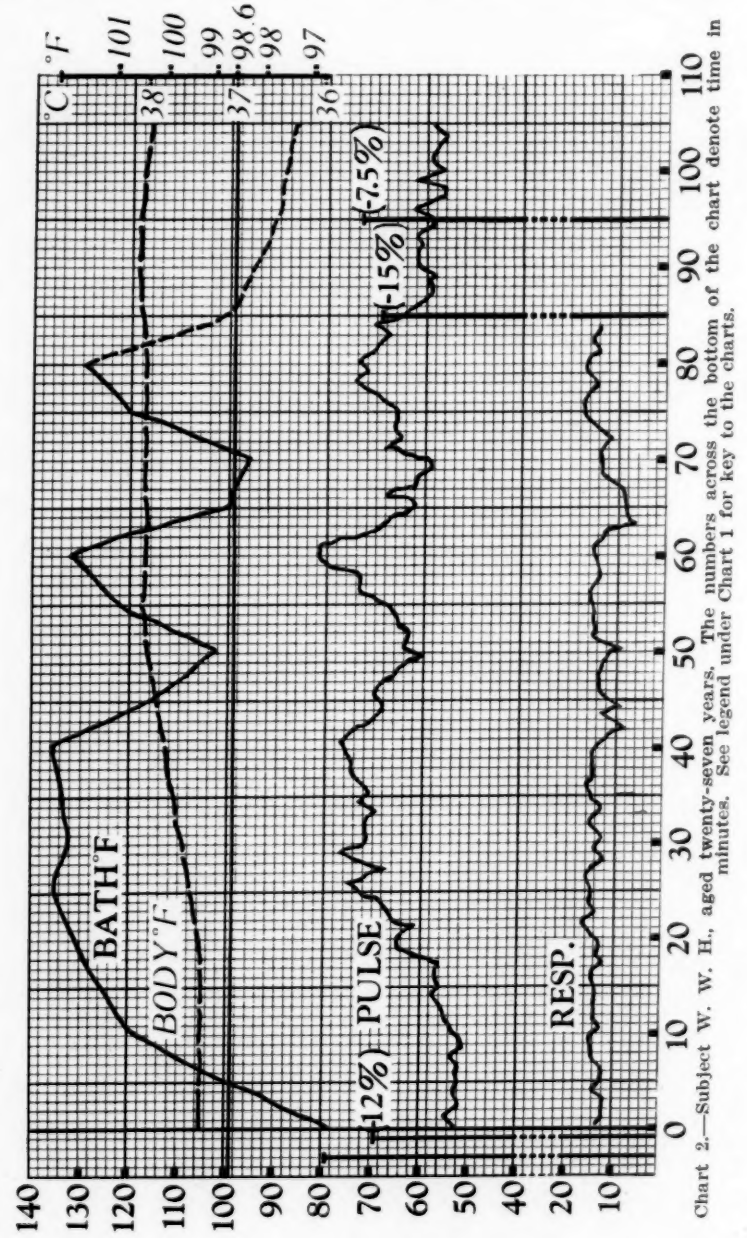


Chart 2.—Subject W. W. H., aged twenty-seven years. The numbers across the bottom of the chart denote time in minutes. See legend under Chart 1 for key to the charts.

The relationships indicated below, were obtained by dividing the change in heart rate, CHR, by the change in bath temperature, CBT, observed during some chosen time period. (The bath temperature is

considered equivalent to the skin surface temperature.) In Chart 1, then, if the increase in heart rate, CHR, during the first twenty-five minutes be divided by the rise in bath temperature, CBT, during the same period, we obtain the following relationship: CHR/CBT = 51/62

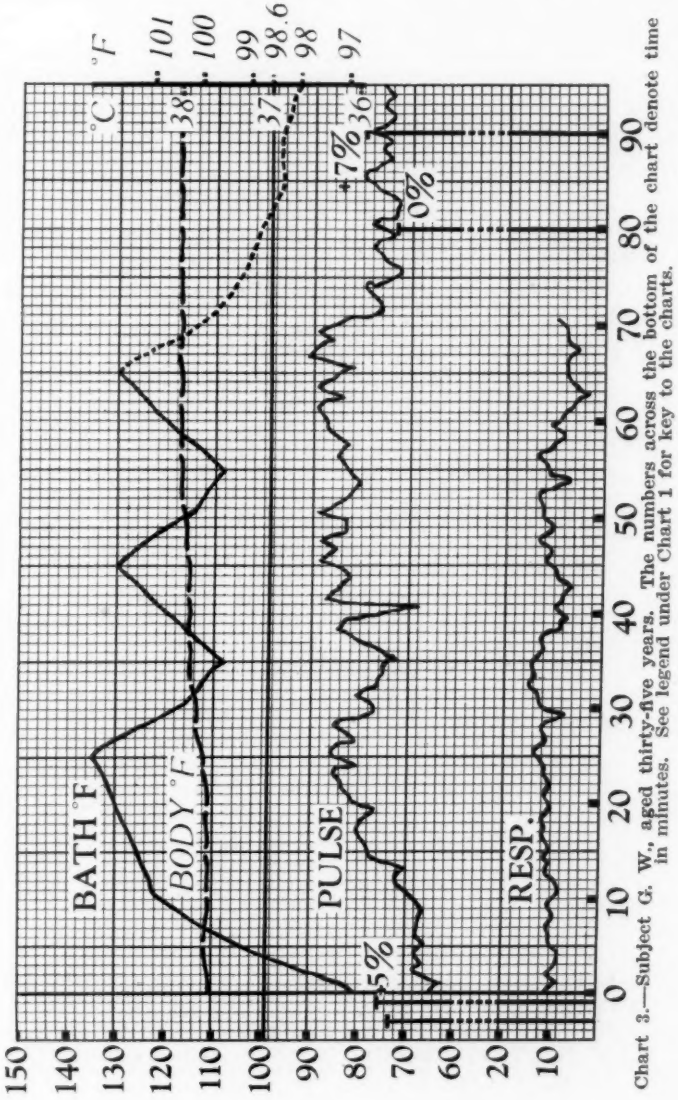


Chart 3.—Subject G. W., aged thirty-five years. The numbers across the bottom of the chart denote time in minutes. See legend under Chart 1 for key to the charts.

= 0.82. That is, as the bath temperature rises one degree Fahrenheit, the heart rate increases 0.82 of one beat.

A similar relationship is also obtained when the bath temperature is lowered: From the 65th to the 75th minute, Chart 1, there is a drop of 26 degrees in the bath (skin surface) temperature, and the heart rate decreases 28 beats. The ratio of CHR/CBT in this case becomes

28/26 = 1.07. This is somewhat higher than the 0.82 obtained above, and the average of the two figures, 0.82 plus 1.07, namely 0.95 is probably the more correct value here. Hence, in the case of this twenty-year-old individual, when he is subjected to a dry air-radiant heat bath, his heart

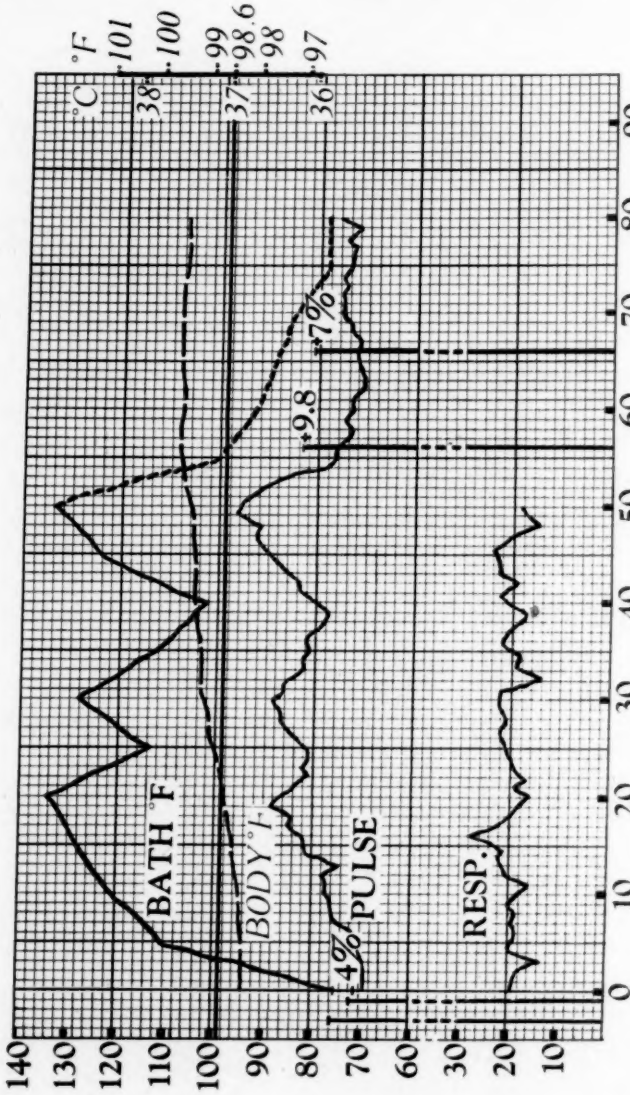


Chart 4.—Subject C. G. H., aged forty-eight years. The numbers across the bottom of the chart denote time in minutes. See legend under Chart 1 for key to the charts.

rate changes about 0.95 of a beat for each degree change in the bath (skin surface) temperature, or almost one beat for each degree.

In the following, all *decreases* in temperature were measured during ten-minute periods, while the *increases* were taken in periods varying from fifteen to forty-five minutes. This is due chiefly to the fact that these experiments were not originally designed for the specific purpose

for which we are using the results here, and the set-up was entirely dismantled before the relationships discussed here were noticed. However, the ratios, CHR/CBT, do not seem to be materially influenced by a difference in time, which, after all, might be expected, since time is not

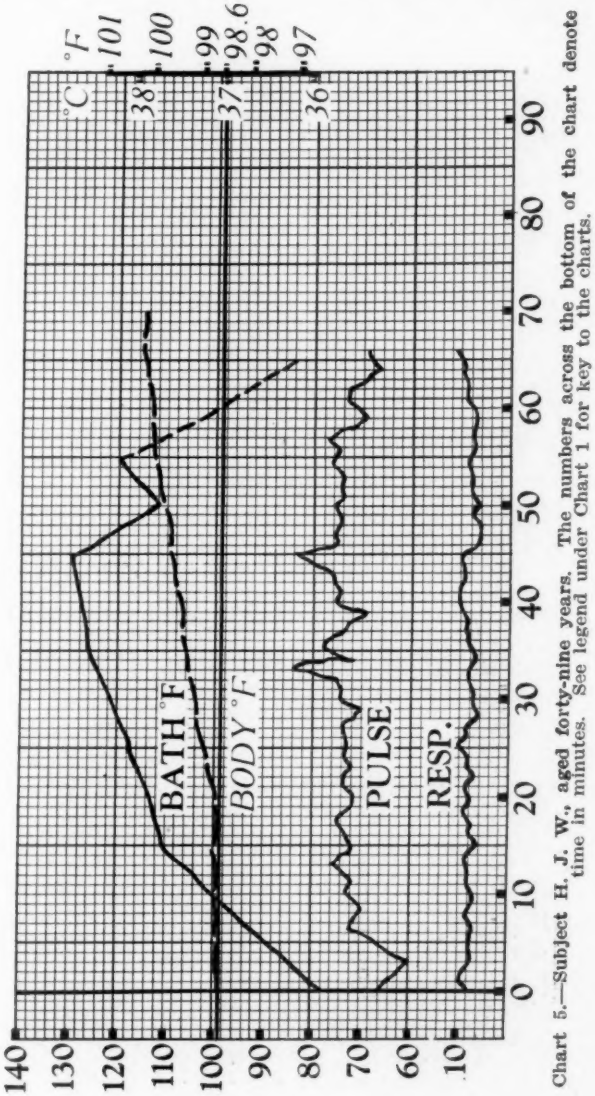


Chart 5.—Subject H. J. W., aged forty-nine years. The numbers across the bottom of the chart denote time in minutes. See legend under Chart 1 for key to the charts.

a factor in the actual calculation. The average time period for the experiments involving increases in temperature, was twenty-eight minutes.

In the tables submitted, the individuals have been grouped according to age: first, those below twenty-five years of age; second, those between twenty-five and forty years; third, those between forty and fifty-five years; and finally those above fifty-five years of age. Had we, at

the time of the experiments, become aware of the relationships indicated below, it goes without saying that more data would have been obtained from older individuals.

Any conclusion to the effect that the indicated influence of age is always present, may be questioned because of the limited number of experi-

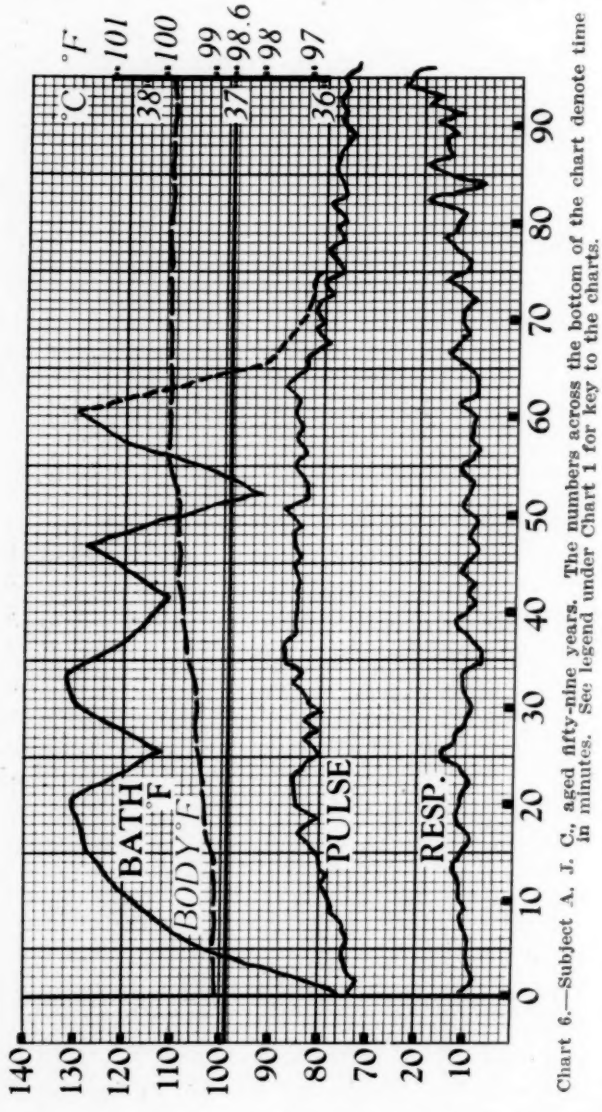


Chart 6.—Subject A. J. C., aged fifty-nine years. The numbers across the bottom of the chart denote time in minutes. See legend under Chart 1 for key to the charts.

ments conducted on older subjects, but it may also be strengthened by stating that in more than 50 experiments run upon younger subjects (athletes), none of them exhibited such a low CHR/CBT value as did the oldest subject—namely, that of 0.161. One of the lowest values obtained on a younger subject was that of 0.325, shown in the above table, on a

twenty-seven-year-old individual, and it is to a large degree upon this indirect support that we have ventured to submit our present deductions.

| | AGE | CHR/CBT | | |
|---|---|---|---|---|
| | 20 | 0.945 | | |
| | 20 | 0.633 | Average: | 0.700 |
| | 25 | 0.520 | | |
| | 27 | 0.325 | | |
| | 34 | 0.504 | | |
| | 36 | 0.502 | Average: | 0.458 |
| | 39 | 0.502 | | |
| | 48 | 0.466 | | |
| | 49 | 0.292 | Average: | 0.325 |
| | 59 | 0.161 | Average: | 0.161 |
| Average: | 35 | 0.485 | | |

On the basis, then, of the above figures, and using the two extreme values of CHR/CBT, namely, 0.945 and 0.161, the efficiency of this skin-heart mechanism is nearly six times greater in an individual twenty years old than it is in one at the age of fifty-nine. A more correct relationship is probably to be obtained by using 0.70 to represent the value of CHR/CBT at the age of twenty, in which case it becomes 4.3 times as great as that in the fifty-nine-year-old individual.

A search of the literature has failed to reveal any information dealing with the problem of the influence of age upon the CHR/CBT ratio, although some such relationship seems to exist in the case of sinus arrhythmia,[1] a heart irregularity found more frequently in younger individuals than in older ones, and thus seems to disappear with the approach of age. In the case of the CHR/CBT relationship we are therefore forced to base our tentative deductions entirely on our own observations and upon the indirect information gathered from the literature. Upon such basis, then, it appears to us that the explanation of this marked influence of age upon the reflex efficiency, as expressed by the term CHR/CBT, may be found in some, or all of the following: (1) Greater power for compensating in the older individual; (2) A decreased efficiency, with age, of the entire reflex arc involved in the reaction; (3) A decreased sensitivity (increased threshold) in the skin temperature receptors themselves; or (4) A thickening, or drying (decreased heat conductivity) of the skin tissue surrounding the temperature receptors.

Of these four suggested explanations, the last one appears to us for the moment as the most plausible. That the threshold of the skin sensory organs increases with the thickness of the skin appears to have been long recognized. In the case of the temperature receptors, Weber[3] attributes the variation in threshold to a decreased heat conductivity due to a thickening of the skin. Adrian[4] draws a somewhat similar conclusion in regard to the sense of touch, the threshold of which depends "on the particular skin surface under the test."

Further substantiation favoring this view, is found in the anatomical condition that "There are, in man, probably no 'end organs' in the

epithelium of the skin . . ." (Waterston[5]). If the latter is correct, it seems quite self-evident that the threshold must increase with any changes in the skin structure—such as increased thickness and dryness—in fact, anything which would tend to decrease the heat conductivity of those parts of the skin which surround the temperature receptors. According to Pütter,[6] water has a heat conductivity of 0.00135, and the dry hide of one of 0.00042; and from this he calculates the heat conductivity of the normal moist skin to be 0.00113, indicating that the heat conductivity of the skin varies directly as the moisture content. The question then arises as to whether or not such a change occurs in the human skin as the individual grows older.

Once the individual has reached maturity, the skin tends to assume a tougher and less elastic structure with increased age. There is a loss of water content which, we are told, is considered one of the chief reasons for the wrinkling of the skin. This water loss may represent but a small portion of the total skin moisture, to be sure; but if, on the other hand, it is derived chiefly from the superficial skin layer covering the temperature receptors, it may dehydrate this layer sufficiently to inhibit markedly the stimulation of the temperature receptors by external heat applications.

Such a dehydrating effect in the superficial skin layer could, in itself, be sufficient, perhaps, to explain the feebler reactions in the older individuals, but it would suffice as an explanation only in case the heat stimulus were of insufficient strength to overcome this increase in skin resistance. Should the heat stimulus be sufficiently intense to penetrate the resistance without a very great proportionate loss of strength, then one should not expect any marked difference in reaction between the moist and dehydrated skins.*

### II. THE COMPARATIVE EFFECT UPON THE HEART RATE OF THE DRY AIR-RADIANT HEAT BATH AND THE WATER BATH, PER DEGREE CHANGE IN TEMPERATURE

In view of the relationship CHR/CBT obtained in the case of the dry air-radiant heat bath, it seemed desirable to determine, if possible, the value of this relationship in the case of the water bath. For such a comparison we have tried to select the data on a basis similar to that

*As for whatever immediate value our deductions may have, we believe it will be of a clinical nature—particularly in the application of heat treatments, as well as of cold packs. Upon the basis of the data submitted, it appears that a heart rate of, say 125, may prove entirely safe in a younger individual, but quite the opposite in a man fifty or sixty years old. In other words, the truest significance of a change in heart rate, when induced by temperature changes, can be best obtained by considering such a change in rate, not only in relation to the magnitude of the temperature change but also in relation to the individual's age on a basis similar, perhaps, to that of blood pressure.

In the case of an increased heart rate from fever of infectious origin, the skin is heated from within by the circulating blood in place of from without by external media. The important factor in either case being the heating of the skin and the accompanying stimulation of the temperature (thermocouple) receptors.

upon which the data for the dry air-radiant heat bath were chosen, and from as many of the same individuals as possible. The most important omission being that the oldest subject, age fifty-nine, had not been used for the water experiments. As in the previous table, the subjects have been grouped according to age:

| | AGE | CHR/CBT | | |
|---|---|---|---|---|
| | 19 | 2.4 | | |
| | 20 | 2.9 | | |
| | 22 | 3.7 | | |
| | 23 | 4.2 | Average: | 3.3 |
| | 24 | 3.3 | | |
| | 25 | 3.3 | | |
| | 26 | 3.7 | | |
| | 27 | 3.8 | Average: | 3.6 |
| | 39 | 3.4 | | |
| | 48 | 2.6 | Average: | 2.6 |
| Average: | 27 | 3.3 | | |

From these results it is quite obvious that, per degree change in temperature, the water bath exerts a much greater influence upon the skin sense organs—and upon the heart rate—than does the dry air-radiant heat bath. Using the average results obtained from each medium, the relationship between their effects on the heart is found to be about seven. That is, $(CHR/CBT)^{w}/(CHR/CBT)^{ha\text{-}rh}$ equals seven. Per degree change in temperature, then, the water bath stimulates the skin sense organs as well as the heart rate, 7 times as much as does the dry hot air-radiant heat bath. In one individual, it was found to be 13 times as great. The possibilities of utilizing this marked difference in physiological effects from the two types of baths, for therapeutic as well as diagnostic purposes deserve a lengthier and more thorough consideration than can be devoted to them here.

In the case of the water bath, there appears no such distinct variation in effect, according to age, as was observed with the dry air-radiant heat bath. As previously indicated, this might be explained by assuming that the stimulation delivered by the hot water is sufficiently powerful to penetrate any increased resistance in the superficial skin layer without much loss of power. In such case, the greater resistance offered by the skin of an older individual would be insufficient to inhibit markedly the stimulation of the temperature receptors, and consequently the value of CHR/CBT would not vary with age. There appears, however, another explanation which, to us, seems equally important, especially if combined with the one already proposed. This explanation is based on the assumption that sufficient water is imbibed by the superficial skin layer to restore its heat conductivity to that of a young moist skin. This would then permit the water to deliver the heat stimulation to the skin sense organs with equal effectiveness in both young and old subjects.

Metabolic tests, when made, were taken just before and after the heat application. These tests, however, give no indication of any direct relationship between metabolism and a rise in body temperature. Indeed, in only one experiment, Chart 1, does the metabolic rate rise definitely above allowable experimental errors, and in this case the increased metabolism seems to be due more to the skin temperature than to the body temperature. One cannot fail to note the sharp contrast in the metabolic changes induced by this form of bath and those reported in our previous article[7] on the cold douche.

## SUMMARY

Under our experimental conditions, the heart rate appears to be not only affected and controlled more by the skin temperature than by the body temperature, but our results also seem to indicate that the acuity and efficiency of this control decrease with the age of the individual, depending to some degree, however, upon the heating medium used.

The efficiency factor has been derived by dividing the "change in heart rate" by the "change in bath temperature," measured in degrees Fahrenheit and is represented by CHR/CBT.

When the heating medium is a hot air-radiant heat bath, the value of CHR/CBT is about 5 times greater in a twenty-year-old individual than it is in one fifty-nine years old. The highest value obtained was from a twenty-year-old individual, namely 0.945, and the lowest value for CHR/CBT was from a fifty-nine-year-old individual, namely 0.161.

Four suggestions are submitted aiming to explain how the efficiency factor CHR/CBT may change in value with the individual's age.

In its effect on the heart rate, the hot water bath is about seven times as stimulating as is the dry air-radiant heat bath. That is, the average derived value of CHR/CBT in the dry air-radiant heat experiments was 0.475 while the average derived value from the water baths was 3.3. The effects of the water bath upon the heart rate do not seem to vary according to the individual's age, as is the case with the effects from the dry air-radiant heat bath. The reason for this appears to lie in the much greater heat stimulation delivered by the water, and to an increased heat conductivity in the superficial skin layer, in turn caused by the imbibition of water by the older dryer skins.

Upon the basis of the results obtained, it appears that the truest significance of a change in heart rate, if induced by temperature changes —water bath excepted—can be best obtained by considering such changes in relation to the individual's age, on a basis similar perhaps, to that of blood pressure.

No definite relationship was observed between the baths and the metabolic rate, and in the few cases in which an increase in metabolism was noted, such an increase seemed to be related more closely to the skin temperature than to the body temperature.

## REFERENCES

1. White, Paul D.: Heart Disease, 1931, The Macmillan Company, pp. 563 and 667.
2. Benson, Simon: Relative Influence of External and Body Temperature Upon the Heart, Arch. Phys. Therapy **15**: 303, 1934.
3. Weber, E. H.: Tastsinn und Gemeingefühl. Rudolph Ostwald's Klassiker der Exakten Wissenschaften Nr. 149, Leipsig, 1905, p. 131. Reprinted from Wagner's Handwörterbuch 111, Nr. 2, 1846, pp. 481 to 588.
4. Adrian, E. D.: The Basis of Sensation, W. W. Norton & Company, Inc., p. 87.
5. Waterston, David: The Sensory Activities of the Skin for Touch and Temperature, Brain **46**: 200, 1923.
6. Pütter, von August: Die Unterschiedsschwellen des Temperatursinnes, Ztschr. f. Biol. **74**: 269, 1922.
7. Benson, Simon, Bergstrom, P. L.: The Scotch Douche and Some Experimental Studies on Its Metabolic Influence, Arch. Phys. Therapy **16**: 327, 1935.

# THE CALCIFIED NODULAR DEFORMITY OF THE AORTIC VALVE*

B. J. Clawson, M.D., J. F. Noble, M.D., and N. H. Lufkin, M.D.
Minneapolis, Minn.

THIS type of cardiac disease, because of its clinical manifestations, frequency, and disputed etiology and pathogenesis, deserves more emphasis than has generally been given to it. It is frequently overlooked, and death often occurs suddenly or without marked symptoms. Many patients are never seen by a physician. Physical findings are not always constant and because of associated cardiac pain the condition is sometimes diagnosed as coronary sclerosis.

Christian[1] in speaking of this form of heart disease thought that it should be recognized clinically more frequently. He referred to it as still being considered relatively infrequently as a possibility in diagnosis. This kind of valvular disease, according to him, is characterized by the following conditions: (1) occurrence chiefly in males relatively late in life; (2) slow progress of the lesion with symptoms of cardiac decompensation appearing late, though not necessarily prolonged after they develop; (3) the presence of a thrill and harsh murmur both systolic in time, often accompanied by a diastolic murmur; (4) considerable hypertrophy of the heart; (5) often a characteristic type of pulse and normal or decreased pulse pressure; (6) the absence of anything in the latter part of the disease throwing light on the etiology; and (7) the finding at autopsy of a very heavy heart with the aortic valve greatly narrowed by thickened cusps often adherent to each other and calcified. The reports of McGinn and White,[2] Boas,[3] and Contratto and Levine[4] agree in general with Christian's findings.

Margolis, Ziellessen, and Barnes[5] found that the most prominent feature in their cases with regard to symptoms was the lack of any characteristic complaints. Often symptoms referable to the cardiovascular system were absent. The findings in the patients who presented themselves with cardiac symptoms were not constant.

The frequency of this kind of heart disease and the means of diagnosing it concern the clinician chiefly. The pathologists are confronted with the task of explaining the etiology and pathogenesis of the condition. This type of valve disease, so commonly seen by the pathologist at autopsy, is obviously frequently not diagnosed clinically.

There are two beliefs concerning the etiology of the calcified nodular deformity of the aortic valve. First, there are those who are convinced

*From the Department of Pathology, University of Minnesota.

that the lesion is degenerative or metabolic in origin. The condition is often called the atherosclerotic valve. The concept of atherosclerosis depends in general on the work of Mönckeberg[6] who after studying aortic valves in which there was extensive calcification decided that the process bringing about the change in the cusps was the same as that found in the intima of the aorta in senile atherosclerosis. He held the opinion that the atherosclerotic process extended directly from the aorta to the valve by way of the sinus of Valsalva. His observations suggested that the change in the cusps was most pronounced at the angle where the cusps and aorta join.

Libman,[7] Ribbert,[8] Geerling,[9] and Soval and Gross[10] agreed with Mönckeberg in considering these deformities degenerative in origin. Soval and Gross recently, after examining hearts with this form of aortic lesion for many stigmata of rheumatic infection, failed to find the stigmata sufficiently constant to consider the change in the valves rheumatic or infectious in origin. These workers concluded that the Mönckeberg aortic lesion is purely and primarily degenerative, its occurrence and extent depending in all probability on individual predisposition to collagen involution and calcium deposition.

Representing the second belief, Clawson[11] from a study of 93 cases decided, from the clinical histories and gross and microscopic structure of aortic calcified valves, that the process is infectious. While atherosclerosis was not infrequently found in valves, especially the mitral, it was concluded that it is doubtful whether deformity severe enough to cause cardiac insufficiency is ever due to a purely degenerative process such as atherosclerosis.

Christian also concluded that the etiological relation of this lesion to rheumatic fever was very probable. Eleven of his 21 cases had a definite history of typical rheumatic fever from thirteen to forty-eight years before the onset of cardiac insufficiency. In two others there was an indefinite history of rheumatism. He consequently stated, "Taking all of this into consideration, a rheumatic etiology would seem highly probable from a study of these histories, a view that I have come to since my statement to the contrary in 1928 in *Oxford Monograph on Diagnosis and Treatment.*" McGinn and White considered it evident that aortic stenosis was doubtless often caused by infection, especially rheumatism. Boas held a similar opinion. Contratto and Levine concluded that rheumatic fever was the most frequent and most important cause of aortic stenosis.

Margolis, Ziellessen, and Barnes apparently were not convinced as to the reliability of either belief. They concluded that the etiology and pathogenesis of these valvular lesions could not be determined with certainty, but that clinical and anatomical data indicated that in some cases the lesions may have an inflammatory basis, whereas in others they may be the result of a noninflammatory degenerative process.

Since these aortic lesions have continued to be a frequent finding in autopsy material at the University of Minnesota and also at other places and because of the diversity of opinion among internists and pathologists concerning the frequency, the clinical course and findings, and the etiology and pathogenesis of these lesions, we decided to restudy our cases of nonsyphilitic aortic valve deformities, the so-called atherosclerotic valve as described by Mönckeberg. This deformity of the aortic valve was called the calcified nodular type by Clawson and Bell[12] in a former paper. This term will be used in a further description of the valve in this discussion.

The group is studied from three angles: (1) clinical characteristics; (2) frequency; and (3) etiology and pathogenesis.

## CLINICAL CHARACTERISTICS

It was not possible to obtain clinical histories of all of our 200 patients. Some had died, others died suddenly without known symptoms and the amount of history obtained from some was too small for use in drawing any conclusions. The things considered in the clinical findings were age, sex, incidence of acute rheumatic fever, rate of development, sudden death, and symptoms and signs, such as dyspnea, precordial pain, thrills, and murmurs.

*Age.*—A clinical characteristic, commonly emphasized, is that the disease is one of old age and that most deaths occur in the older decades. The youngest in Christian's series of 21 patients was 30 years; 13 were over fifty and 7 over sixty; only 8 were under fifty. In the series of 41 reported by Margolis, Ziellessen, and Barnes only 3 were under forty years, 3 between forty and forty-nine, and 35 were fifty or more years old. Cabot's series[13] of 27 showed 5 to be under forty years, 7 between forty and forty-nine, and 15 over fifty. It is seen in the total of these three series (89) that the majority of the patients lived to be fifty years or older. McGinn and White found their cases to be chiefly older persons. The ages in the 180 cases reported by Contratto and Levine ranged from thirteen to eighty-one years. The largest number occurred in the sixth decade.

We had 200 patients in our series. The ages are recorded in percentages in Fig. 1. One per cent of the cases was in the second decade, 6 per cent were in the third decade, 13.5 per cent in the fourth, 18.5 per cent in the fifth, 22 per cent in the sixth, 22.5 per cent in the seventh, 14 per cent in the eighth, and 2.5 per cent in the ninth. Seventy-nine per cent of the patients were fifty or more years old. The greatest number was in the seventh decade. Our findings agree with those of other observers in showing that this kind of aortic valvular lesion is found chiefly in older people.

*Sex.*—It has repeatedly been pointed out that the calcified deformity of the aortic valve predominates in males. Fifteen of Christian's 21 cases were found in males. In Cabot's series 25 of 28 and in that of Margolis, Ziellessen, and Barnes 34 of 42 were males. Males also predominated in the cases reported by McGinn and White and by Contratto and Levine.

We have found this greater preponderance of males to be present in our material. In 200 cases of what in our opinion would pass as the Mönckeberg aortic valve disease 165 were in males and 35 were in females. This does not give the proportion which should be expected in a cross section of the population in this locality dying with this disease, for the proportion of males to females in our autopsy material in the decades in which most of the patients died is 2 to 1. In a series of 15,937 autopsies studied by McCartney (personal communication) the number of males and females in the first three decades were practically equal. The fourth to the seventh decades, inclusive, showed the ratio of males to females to be approximately 2 to 1. Our cases of calcified aortic valve deformities should accordingly be about 165 males to 70 females, which shows the males still to be much more common in the group, a ratio of slightly over 2 to 1.

*Rheumatic Fever.*—In discussing the characteristics of this group, Christian gave as one point a history of rheumatism in early life. Such a history was present in 11 of his 21 cases. The rheumatic attacks occurred from thirteen to forty-eight years before the onset of cardiac insufficiency. Some had repeated attacks. A history of rheumatic fever was obtained in 23 per cent of autopsied cases and in 46 per cent of the clinical series reported by McGinn and White. Contratto and Levine found a definite history of rheumatism in 31.7 per cent of their cases. Evidences of one or more attacks of acute rheumatic fever were frequent in our series; a positive history was reported in 35 per cent. The frequency was great enough to suggest strongly a causal relationship. This is discussed more in detail under etiology.

*Rate of Development.*—Christian's observation that this type of aortic valve deformity develops slowly was confirmed by the clinical and pathological findings in our material. This slowness was particularly indicated by the length of time between the last attack of rheumatism and the beginning of clinical symptoms, by the large amount of calcium in the cusps and by the smooth condition of the intima of the aorta (described more fully under etiology).

*Sudden Death.*—The frequency of sudden death has been emphasized by Marvin and Sullivan,[14] by Margolis, Ziellessen, and Barnes, and by Laplace.[15] We found that sudden death occurred in 15 per cent of our 200 cases. This frequency may be unduly high, as the coroner's

autopsies were included in our material. The calcified aortic heart disease has to be considered with coronary sclerosis and syphilitic aortitis as a medicolegal cardiac case.

*Symptoms and Signs.*—One hundred cases with fairly good histories were selected for a study of clinical symptoms and signs.

Dyspnea was the most common symptom noted. It was present in at least 95 cases, absent in 1 and not mentioned in 4. The dyspnea was regularly of a severe degree and was frequently of long duration. Death sometimes occurred in an attack. Severe orthopnea was of common occurrence.

Laplace, Boas, and Contratto and Levine have emphasized the common occurrence of anginal attacks associated with aortic stenosis. Angina was a commonly recorded symptom in our cases. It was reported present in 42, absent in 6, and was not mentioned in 52. Coronary sclerosis was sometimes diagnosed. The theories offered to account for this cardiac pain have been interesting. Laplace, after studying the relation of blood pressure to angina, decided that a low diastolic pressure was of slight importance in the pathogenesis of angina pectoris. Boas concluded that the angina was due to the narrowing of the aortic valvular opening itself which impaired the blood supply to both coronary arteries simultaneously. Contratto and Levine thought the stenotic aortic orifice acted upon the coronary arteries in a manner similar to a common water faucet suction pump to draw blood out of the coronary arteries. A possible explanation of this pain in some cases is offered in connection with the description of the structure of the aortic cusps.

Murmurs were reported as being present in 84 of 100 cases, 30 times as both systolic and diastolic, 45 times as systolic only, and 6 times just as murmurs. In 6 cases murmurs were reported to be absent. No mention of them was made in 10.

Thrills were not so common. They were reported present in 29 and absent in 29; they were not mentioned in 42. In nearly all cases in which thrills were absent or not mentioned, findings relative to murmurs were reported.

The blood pressure readings were analyzed in 90 of our more recent cases. The following is a summary of these blood pressure readings:

| *Height* | *Number* | *Pulse Pressure Above 65* |
|---|---|---|
| (95-150/60-90) | 57 | 7 |
| Above 150/60-90 | 10 | 8 |
| Above 150/above 90 | 10 | 8 |
| Below 150/above 90 | 2 | 0 |
| Above 95/below 60 | 5 | 5 |
| Below 95/70 or less | 6 | 0 |
| Total | 90 | 28 |

Twenty of these 90 patients had a systolic pressure of over 150 and 12 had a diastolic pressure above 90. Only about 10 could be placed in the hypertensive group.

A pulse pressure of 65 or more was noted in 28 patients, usually in those with the higher readings. The pulse pressure except in a few cases was not much in excess of 65. Twelve had pulse pressures ranging from 65 to 74, eight from 75 to 84, 3 from 85 to 94, 2 from 95 to 104, one from 105 to 114, and two 155 or above.

Thirty of the 90 cases had pulse pressures which ranged from 45 to 64, about a normal reading, and 32 had pulse pressures below 45, 14 from 35 to 44, 10 from 25 to 34, 6 from 15 to 24, and 2 from 5 to 14. In general it was found that the greatest pulse pressure was in cases with less stenosis but this was not a universal finding. A high pulse pressure was not a characteristic finding in the group. Most cases had normal or low blood pressures and pulse pressures.

The clinical findings agreed in general with those reported by Margolis, Ziellessen, and Barnes, Christian, McGinn and White and Contratto and Levine except in the constancy of the presence of thrills and murmurs.

Congestive heart failure was determined by the presence of edema (indicated by anasarca, hydrothorax, or ascites) and passive congestion of the liver. Edema was noted in 75 per cent of the 200 cases and chronic passive congestion of the liver in 80 per cent.

The weight of the hearts ranged from 400 grams to 1150 grams. Most of the hearts weighed from 500 to 800 grams.

The group clearly may be considered a clinical entity. The sex and age distribution, the frequency of precordial pain and sudden death differentiate the group clinically from other forms of valve disease. Whether the group should be considered an etiological entity is discussed further under etiology.

## FREQUENCY

The frequency of the calcified nodular deformity of the aortic valve concerns the clinician primarily. It has been emphasized by all the reports on this form of valve disease. The lack of a proper knowledge of the frequency of the lesion is, no doubt, the cause of some mistakes in diagnosis. The pathologist is forced to believe that adequate emphasis has not been placed upon the frequency of aortic valve lesions.

Six hundred and thirty cardiac deaths classed as rheumatic valvular disease (the calcified nodular aortic group included) were studied. These were classed as follows:

| | | |
|---|---|---|
| 1. Acute rheumatic | 78 | 12 per cent |
| 2. Recurrent rheumatic | 62 | 10 per cent |
| 3. Healed valve deformities | 490 | 78 per cent |
| a. Calcified aortic | 200 | 41 per cent |
| b. Other healed valve deformities | 290 | 59 per cent |

The calcified nodular group comprized 41 per cent of all healed valve deformities or about 31.5 per cent of all rheumatic heart disease. The frequency of the calcified aortic valve deformity among the healed valve defects may be summarized as follows:

1. Total number of healed valve deformities, 490.
2. Aortic valve involved in 265, 54 per cent.
3. Number of calcified nodular aortic valve deformities, 200, which equals 75.5 per cent of all healed aortic valves.
4. Twenty-three of the remaining 65 aortic valve deformities are described as containing calcium.
5. Eighty-four per cent of all nonsyphilitic aortic valve deformities in our autopsies are described as containing calcium by gross examination.
6. The healed deformed aortic valve, a very common condition, regularly becomes calcified.
7. The calcified nodular deformity is the most common and the usual healed lesion of the aortic valve. Its importance is obvious.

## ETIOLOGY

The etiology of this valve deformity was studied from two angles: (1) the infectious, and (2) the metabolic. The first is referred to as infectious or rheumatic and the latter as metabolic, degenerative, or atherosclerotic. An attempt is made to find evidence for and against each side. The etiological factors studied were age, sex, history of rheumatism, frequency of adherent pericardium, gross structure of the valves, microscopic structure of the valves and myocardium, gross appearance of the aortas, and the expectancy of healed rheumatic aortic valve deformity.

*Age.*—As was pointed out in studying age (Fig. 1) in its relation to the calcified aortic valve disease, it was found that the large majority of patients were old persons. Seventy-nine per cent of our cases were fifty years old or older. The largest number was in the sixth and seventh decades. Since atherosclerosis is a disease primarily of older people it becomes natural to think that the calcified aortic valves are also atherosclerotic in origin.

But, while it is true that the majority was found to die in upper age decades, it seems to us after analyzing our cases that the old age of this group has been somewhat overemphasized, especially as to etiological significance. Twenty-nine per cent of the patients were not over forty years old. Four per cent were not over twenty years old. An attempt was made in analyzing our cases to explain why people dying with this lesion are as a rule old.

In a previous study of healed valve deformities we[12] found that patients with an aortic lesion only, lived longer than those with a mitral

lesion. The ages of the 89 in the group of 200 cases of calcified nodular aortic valve deformity which had a mitral lesion also were studied and compared with the ages at which death occurred in the other cases of healed valve deformities.

Fig. 1 shows the decades in which death took place in the 89 members of the calcified aortic group with a mitral valve deformity also. It was seen that the peak of the occurrence of death dropped from the seventh decade in the total group of 200 to the fifth decade, a difference of

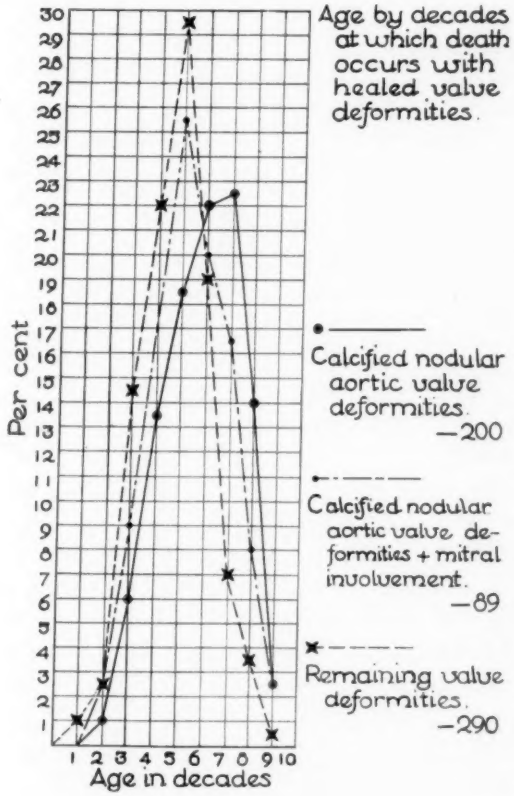
Per cent
Age in decades
Age by decades at which death occurs with healed valve deformities.
Calcified nodular aortic valve deformities —200
Calcified nodular aortic valve deformities + mitral involvement. —89
Remaining valve deformities. —290

Fig. 1.

twenty years. It was also found that the greatest number of this group of 89 died in the same decade, the fifth, in which the greatest number of the remaining old valve deformity patients died. These latter are generally accepted as being of rheumatic origin. It seems reasonable to conclude that the explanation of the fact that most members of the calcified aortic group die in the older decades is that most of these people have aortic lesions alone. They live longer because they have aortic lesions rather than having aortic lesions because they are old. The fact that the members of this group are old offers no reason for believing

that the lesions in the valves in the group must be due to an etiological agent different from the agent causing the lesions in the commonly observed calcified mitral valve deformities.

*Sex.*—It was noted (Table I) that most people dying with a calcified aortic valve disease were males. This fact seems to have little or no significance from the etiological point of view. Atherosclerosis is of

TABLE I

SEX INCIDENCE IN RHEUMATIC HEART DISEASE, 630 PATIENTS

| KIND | MALES | FEMALES | FEMALES CORRECTED |
|---|---|---|---|
| Acute rheumatic | 36 | 42 | |
| Recurrent rheumatic | 31 | 31 | 46 |
| Calcified nodular aortic deformity | 165 | 35 | 70 |
| Other healed valves | 145 | 145 | 290 |
| Total | 377 | | 406 |

about the same frequency in both sexes, though in our autopsy material death from coronary sclerosis is more common in males. The preponderance of males in this group, we think, can be explained by studying the combinations of valve involvement as related to age and sex.

The incidence of males and females in all classes of rheumatic heart disease is shown in Table I. In the acute rheumatic group (78) there were 36 males and 42 females. No correction was necessary between the sexes in this group since its occurrence was in the lower decades. Of the 62 patients dying with recurrent rheumatic endocarditis 31 were males and 31 females. This required slight correction to give a cross section of the population dying with this condition. As corrected there were 31 males and 46 females. The calcified nodular aortic group as corrected was distributed as 165 males and 70 females. The other healed valve deformities were 145 males and 290 females. The total was in the proportion of 377 males to 406 females, close to an equal distribution.

The outstanding things noted in the sex distribution in these heart diseases are: (1) males predominate in the calcified aortic group, and (2) females predominate at nearly the same ratio in cases of other healed valve deformities. These findings, we think, can be partly explained in studying the combinations of valve involvement in the rheumatic heart diseases as related to age and sex. Three combinations were studied: (1) aortic valve alone, (2) mitral valve alone, and (3) aortic and mitral valves combined.

The combinations in acute and recurrent rheumatic valvulitis are shown in Table II. The aortic valve alone occurred three times in males and not at all in the females. The mitral valve alone was present 32 times in males and 41 times in females. The aortic plus mitral combination was found 32 times in each. In this younger group it is seen

TABLE II

COMBINATIONS OF VALVE INVOLVEMENT BETWEEN THE SEXES IN ACUTE AND RECURRENT RHEUMATIC VALVULITIS, 140 PATIENTS

| KIND | MALES | FEMALES |
|---|---|---|
| Aortic alone | 3 | 0 |
| Mitral alone | 32 | 41 |
| Aortic + mitral | 32 | 32 |
| Total | 67 | 73 |

that there appears to be a beginning of a preponderance of aortic valve involvement alone in males and a preponderance of mitral valve involvement alone in females.

These ratios of preponderance continued to increase in the older group as shown in Table III. In this group there were 490 cases of

TABLE III

COMBINATIONS OF VALVE INVOLVEMENT BETWEEN SEXES IN ALL HEALED VALVE DEFORMITIES, 490 PATIENTS

| KIND | MALES | FEMALES | FEMALES CORRECTED | |
|---|---|---|---|---|
| Aortic alone | 113 | 19 | 38 | 3 to 1.0 |
| Mitral alone | 91 | 110 | 220 | 1 to 2.5 |
| Aortic + mitral | 107 | 50 | 100 | |
| Total | 311 | | 358 | |

healed valve deformities. Because of the decades in which death occurred the autopsy records required a correction of males to females to a ratio of 2 to 1. The combination of aortic valve involvement alone was present as 113 males to 38 females, a ratio of 3 to 1. The mitral valve alone involvement was 91 males to 220 females, a ratio of 1 to 2.5. The aortic plus mitral combination, as with acute and recurrent rheumatic valvulitis, was practically equal. The things noted were the marked preponderance of the aortic involvement in males and mitral involvement in females. The explanation of this reverse ratio is not apparent in these figures.

It was found in a previous publication that an individual with an aortic lesion would survive from fifteen to twenty years longer than one with a mitral lesion. This is probably due to the greater ability of the left ventricle to withstand strain. The fact that aortic involvement predominates in males and the mitral involvement in females and that individuals with aortic lesions live longer than those with mitral lesions offers an explanation of the preponderance of males in the calcified nodular aortic group. This explanation appears to us to be more justifiable than to assume different etiological agents in the calcified group and the group including all other healed valve deformities in the absence of a structural basis for considering them separate entities. There appears to be no basis for considering the preponderance of the male sex an etiological factor in this calcified aortic group.

*Evidence of Previous Attacks of Rheumatism.*—In studying the evidences of the occurrence of previous rheumatic infections in our cases five things were considered: (1) a history of rheumatism; (2) the presence of an adherent pericardium; (3) an associated mitral or other valve involvement; (4) associated gross active lesions such as acute rheumatic or bacterial vegetations on the aortic or other valves; and (5) microscopic stigmata of rheumatic inflammation in the myocardium. The findings of these five types of evidence are summarized in Table IV.

TABLE IV

EVIDENCES OF THE OCCURRENCE OF RHEUMATIC FEVER IN CASES WITH CALCIFIED NODULAR AORTIC VALVE DEFORMITY

(A) HISTORY OF RHEUMATISM AND THE PRESENCE OF PERICARDITIS

| KIND OF VALVE DEFORMITY | NUMBER | POSITIVE HISTORY | PERICARDITIS | ONE OR BOTH |
|---|---|---|---|---|
| Calcified nodular aortic | 200 | 35 per cent | 16 per cent | 41 per cent |
| Other healed valves | 160 | 41 per cent | 18 per cent | 49 per cent |

(B) ASSOCIATED MITRAL OR OTHER VALVE DEFORMITY

| KIND | NUMBER | MITRAL OR OTHER VALVE DEFORMITY |
|---|---|---|
| Calcified nodular aortic | 200 | 44.5 per cent |

(C) ASSOCIATED GROSS ACTIVE LESIONS ON VALVES

| KIND | NUMBER | ACUTE RHEUMATIC | BACTERIAL | TOTAL |
|---|---|---|---|---|
| Calcified nodular aortic | 200 | 8.5 per cent | 4 per cent | 12.5 per cent |

(D) MICROSCOPIC FINDINGS IN MYOCARDIUM

| KIND | NUMBER | ASCHOFF NODULES | IRREGULAR INFLAMMATION | TOTAL |
|---|---|---|---|---|
| Calcified nodular aortic | 54 | 13 per cent | 24 per cent | 33 per cent |
| Other healed valves | 68 | 13 per cent | 20 per cent | 28 per cent |

In 200 cases of the calcified aortic valve deformities a *history of rheumatism* was found in 35 per cent, the infection occurring as a rule many years before cardiac symptoms appeared. In 160 cases of other healed valve deformities a history of rheumatism was recorded in 41 per cent, a figure only slightly higher than that in the calcified aortic group. Several factors might account for the slightly lower incidence of a history of rheumatism in the calcified aortic group. A greater number die suddenly without any clinical history being recorded. A diagnosis of valvular disease has less commonly been made and consequently a history of rheumatism might not have been sought. Then, as pointed out by Christian, many of these people are old and do not remember having had an attack of acute rheumatic fever.

The presence of an *adherent pericardium* is significant in these cases (Table IV). Not including tuberculous pericarditis and pericardial adhesions associated with coronary thrombosis and infarction, the conspicuous cause of an adherent pericardium in autopsy material is a

previous rheumatic infection. It is seldom found without an associated valvular involvement. The frequency of an adherent pericardium was compared in this group of 200 cases of calcified aortic valve deformity and 160 other cases of healed valve deformities. Adherent pericardium was present in 16 per cent of the former and in 18 per cent of the latter. A history of rheumatism or an adherent pericardium or both was present in 41 per cent of the cases of the calcified aortic valve deformities and in 49 per cent of the other healed valve deformities. This degree of frequency of rheumatic history and adherent pericardium strongly suggested more than a coincidental relation beween rheumatic infection and the calcified nodular aortic valve deformity. So high a percentage could not be found in nonrheumatic groups.

The association of a mitral or other valve deformity with the calcified aortic valve was present in 44.5 per cent of the 200 cases. There was also an association of acute rheumatic vegetations on the aortic cusps or on the cusps of other valves in 8 per cent. The bacterial type of vegetations was noted in 4 per cent. A total incidence of one or other of the active lesions was seen in 12.5 per cent (Table IV).

The myocardium was examined microscopically for rheumatic stigmata in 54 cases of the calcified nodular aortic group and in 68 cases of the other valve deformities (Table IV). Aschoff nodules were present in 13 per cent of each. Irregular inflammation was observed in 24 per cent of the former and in 20 per cent of the latter. A total evidence of inflammation was noted in 33 per cent of the calcified aortic group and in 28 per cent of the other group of healed defective valves.

The valves in the group of calcified nodular deformity were studied by gross and microscopic examination to find evidences for or against the inflammatory and degenerative origins of the changes. The following gross features were observed; (1) degree of diffuse thickening of the cusps, (2) the degree of stenosis, (3) the frequency of fusion of the cusps, and (4) the relative frequency of the calcified nodules on the aortic and ventricular surfaces of the cusps.

The degree of thickening of the cusps was expressed in grades +, ++ and +++. One plus indicated only slight thickening; three plus was an extreme grade and ++ was intermediate. One hundred and six hearts were available for this examination (Table V). No diffuse thickening

TABLE V

DEGREE OF DIFFUSE THICKENING OF AORTIC CUSPS IN CASES OF CALCIFIED NODULAR AORTIC VALVE DEFORMITY

| NUMBER | DEGREE OF THICKENING | PER CENT |
|---|---|---|
| 106 | 0 | 2 |
| | + | 15 |
| | ++ | 41 |
| | +++ | 42 |
| | Fusion of cusps | 90 |

was noted in 2 per cent. Grade + was present in 15 per cent, grade ++ in 41 per cent and grade +++ in 42 per cent. A severe degree of thickening of the cusps was noted in 83 per cent of the cases. The edges of the valves were fused in 90 per cent of the cases.

The amount of stenosis observed was also expressed in grades +, ++, and +++. The same 106 hearts were examined for stenosis (Table VI).

TABLE VI

DEGREE OF AORTIC STENOSIS IN CASES OF CALCIFIED AORTIC NODULAR VALVE DEFORMITY

| NUMBER | DEGREE OF STENOSIS | PER CENT |
|---|---|---|
| 106 | 0 | 8.5 |
| | + | 20.0 |
| | ++ | 26.5 |
| | +++ | 45.0 |

No stenosis was present in 8.5 per cent. There was grade + in 20 per cent, grade ++ in 26.5 per cent and grade +++ in 45 per cent. Stenosis considered to be of sufficient severity to be observed clinically was present in 71.5 per cent.

The location of the calcified nodules on the valves has much significance in interpreting the pathogenesis of the calcified aortic valve. The acute verrucous vegetations regularly are found on the ventricular surface of the aortic cusps. The calcified nodules should be on the same side if the nodules are calcified vegetations. If the nodules are atherosclerotic in origin they naturally would occur on the aortic surface of the cusps. Mönckeberg believed the nodules developed in the fibrosa layer, having progressed from the aorta by way of the sinus of Valsalva. In this case the nodules being located on the aortic surfaces would suggest the atherosclerotic origin more than the inflammatory origin.

One hundred and six hearts were examined to determine the location of the nodules (Table VII). In 11 per cent the nodules were found

TABLE VII

LOCATION OF CALCIFIED NODULES ON AORTIC CUSPS

| NUMBER | AORTA SURFACE ALONE | VENTRICULAR SURFACE ALONE | BOTH |
|---|---|---|---|
| 106 | 11 per cent | 1 per cent | 88 per cent |

on the aortic surface alone. They were on the ventricular surface alone in only one per cent of the cases. In the remaining 88 per cent calcified nodules were found on both surfaces of the cusps. These nodules are certainly not calcified vegetations. They have the gross appearance of being calcified nodular masses in the diffusely thickened valves. Their size and frequent location on the aortic surface make it possible for them

to impinge upon the orifices of the coronary arteries in some cases. It seems possible that this may in some cases be a factor in the common occurrence of angina in this group.

The microscopic findings in the cusps of these calcified aortic valves are very important in suggesting the etiology of the lesions. Two stigmata of rheumatic infection, only, were considered, exudative or proliferative inflammation and the presence of blood vessels in the cusps and rings. The cusps from 74 cases were examined microscopically (Table VIII). A definite inflammatory reaction was noted in 69 per

TABLE VIII

MICROSCOPIC FINDINGS IN THE AORTIC VALVE IN CASES OF CALCIFIED NODULAR AORTIC VALVE DEFORMITY

| NUMBER | INFLAMMATION, PROLIFERATIVE OR EXUDATIVE | BLOOD VESSELS, VALVE-RING OR BOTH | TOTAL |
|---|---|---|---|
| 74 | 69 per cent | 95 per cent | 97 per cent |

cent. The type of reaction was mostly proliferative. It may be believed, of course, that this inflammation is a foreign body reaction to the calcium. Against this is the fact that calcium was present in all cases but evidence of an active inflammatory reaction was found in only 69 per cent of the cases. It was also noted that the position of the inflammatory reaction bore no immediate relation to the position of the calcium. Often the most pronounced inflammation was seen in parts of the scar where there was no calcium. The calcium was imbedded in a scar much of which was old and healed. The amount of active inflammation was practically the same as that seen in healed thickened mitral valves.

Whether blood vessels are present in normal valves has been a point of disagreement among workers for several years. Gross,[16] who has studied this subject extensively, has decided that blood vessels are not present in normal valves. All observers agree that vessels are not found by microscopic examination in the normal valves. There is not a general agreement on whether vessels may be demonstrated by injecting the valves. Seventy-four of these thickened aortic valves were examined and definite blood vessels were observed in the cusp or ring or both in 95 per cent of the cases (Table VIII).

In the 74 hearts 97 per cent showed evidence of inflammation by the presence of an inflammatory reaction or blood vessels in the valves or valve rings or by both.

Cholesterol crystals so commonly seen in atherosclerosis were not seen in any of the valves. Lipoid material in small amount was sometimes seen.

Another gross observation made referable to etiology, was the smooth condition in the intima of the arch of the aorta in these cases. If the

lesions in the valves are atherosclerotic in nature and are extensions from the intimal change in atherosclerotic aortas, one should find considerable intimal change in the aortas of this group. The arches of the aortas were examined in 106 hearts (Table IX). In 86 per cent there was no sclerosis

TABLE IX

DEGREE OF ATHEROSCLEROSIS IN AORTA IN CASES OF CALCIFIED NODULAR AORTIC VALVE DEFORMITY

| NUMBER | NONE TO A TRACE | MODERATE | EXTREME |
|---|---|---|---|
| 106 | 86 per cent | 14 per cent | 0 |

or only a trace. Fourteen per cent showed a moderate amount of intimal atherosclerosis. Extensive atherosclerosis was not seen in any. The smoothness of the arches of the aortas in these cases was a conspicuous finding. No other group of individuals in the same decades of age could be found with so little atherosclerosis. In fact, it seems evident that these aortas have been protected by the stenosis of the aortic orifice and since the smoothness corresponds to that in young people, it is strongly suggested that the deformities in the cusps in most cases began early in life and have been present a long time. This pathological inference is in harmony with the clinical observations noted by many. This anatomical observation not only indicates an early occurrence of the change in the valve but it fails to support the idea that the valvular lesion is atherosclerotic in origin.

Another approach to the study of the etiology of these calcified aortic cusps is to study the expectancy of healed valve deformities from the incidence of acute and recurrent valvulitis both of which, of course, are obviously of rheumatic origin. An illustration of this study is seen in Fig. 2.

Exclusive of syphilitic and bacterial valvulitis there were 630 cases of valvular disease (acute rheumatic valvulitis, recurrent rheumatic valvulitis and healed valvular deformities). The acute and recurrent rheumatic cases (140 in number) were placed in one group since there can be no doubt about the rheumatic etiology. The total healed valve deformities (490 in number) were placed in a second group. The frequency of aortic involvement was studied and compared in the two groups.

In the acute and recurrent rheumatic group the aortic valve alone was involved in 2.1 per cent of the cases. The total aortic involvement in this group was 49.2 per cent. In the group of healed valves the aortic valve alone was involved in 26.3 per cent and the total aortic involvement was 59.1 per cent of the 490 cases.

The healed valve group had a 10 per cent greater incidence of aortic involvement than the acute and recurrent rheumatic group. This dif-

ference can probably be accounted for by the increase with age in the involvement of the aortic valve alone. The chance of aortic involvement alone increases with age as shown in Fig. 2. In this chart it is seen that the individuals in the healed valve group had an average age of about thirty years older than those in the acute and recurrent rheumatic group. It appears evident that the incidence of the total healed aortic valve deformities is practically what should be expected from the incidence of aortic involvement in known cases of rheumatic infection. If the calcified aortic group (200) were taken out of the total healed valve group (490) it would leave a relatively small number (87) having an

Aortic involvement at death.

| Kind | Number | Aortic alone | Total aortic |
|---|---|---|---|
| Acute and recurrent rheumatic | 140 | 2.1 % | 49.3 % |
| Total healed valve deformities | 490 | 26.3 % | 59.1 % |

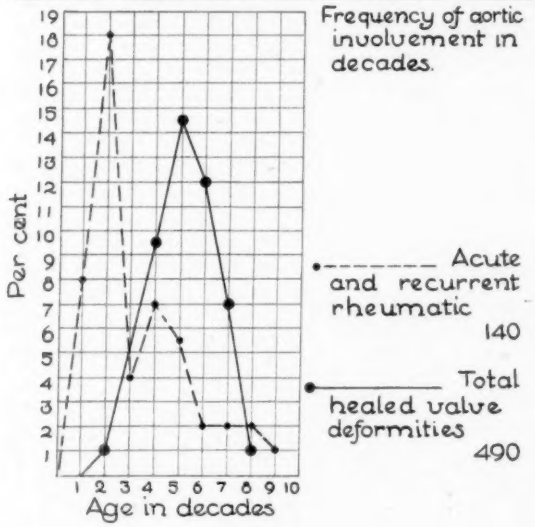


Fig. 2.

aortic lesion. The number with aortic involvement would be much below what should be expected. There seems to be no reasonable necessity to look for a nonrheumatic cause of the calcified aortic valve deformities.

## COMMENT

The calcified aortic valve deformity is a condition which is being recognized and emphasized more by both internists and pathologists. The condition has come to be looked upon as a clinical entity. This is primarily because of certain common clinical manifestations, such as being more common in males and in the older groups. It is also characterized by the clinical symptoms often appearing many years after the probable

beginning of the disease. The pulse pressure commonly is not high. It carries with it a better prognosis than a mitral disease, since the right ventricle is not handicapped so easily. It has to be differentiated from coronary sclerosis on account of the common occurrence of angina and sudden death.

Physical findings when present are fairly characteristic but are not always constant.

The fact that this type of aortic valve disease is a clinical entity does not necessarily indicate that it is an etiological entity.

Aortic valve disease, especially calcified aortic stenosis, is a much more common condition than has been generally believed. The condition is being diagnosed clinically much more frequently than was done ten to fifteen years ago. It is much more common than a nonsyphilitic aortic valve deformity without calcium. In fact, calcification is the usual finding in a healed scarred aortic valve.

The exact etiology and pathogenesis of this type of lesion cannot be proved conclusively any more than the etiology and pathogenesis of the sclerotic and calcified mitral valve in which calcification is practically as common. The origin of the mitral deformity is generally accepted by most students of the subject to be due to previous and probably repeated rheumatic infections which cause a proliferative inflammation which terminates in a scar. It is not unreasonable to accept the same explanation for the etiology and pathogenesis of the calcified aortic lesions.

Two theories are advanced to explain the origin of these calcified aortic valve lesions; (1) the metabolic, degenerative or atherosclerotic, and (2) the infectious or what is generally called rheumatic.

The age of most of the individuals in the group, sixth and seventh decades, has supported the atherosclerotic theory in the opinion of many. On the other hand it has to be remembered that this is an aortic lesion and people with aortic lesions live longer than those with mitral lesions. It was found that those in the calcified aortic group who had mitral lesions also died, as a rule, in the same decades as other cases of healed valvular deformities which are commonly recognized as being due to rheumatic infection.

The greater number of people having this calcified aortic valve deformity are males, a fact also sometimes considered to be in favor of the atherosclerotic theory of etiology. This also fails to have much weight when it is remembered that females have atherosclerosis about as commonly as males and also that the aortic valve involvement is more common in males than in females and the mitral valve involvement is more common in females than in males. The males having the preponderance of aortic valve involvement live longer, and the females with the pre-

ponderance of mitral involvement die earlier and thus the calcified aortic valve deformity becomes a disease of males primarily in the older groups.

The rheumatic origin of this calcified aortic lesion is strongly supported by the various evidences of one or more attacks of acute rheumatic fever in the members of the group. A positive history of rheumatic fever was practically as common in this group as in other cases of healed valve deformity. The presence of an adherent pericardium was essentially the same as in cases with other healed valve defects generally recognized as being rheumatic. Aschoff nodules and other microscopic stigmata of rheumatic inflammation were found with equal frequency in the group with the calcified aortic cusps and in the group with healed valve deformities not so classified.

The gross structure of the aortic valves was not characteristic of an atherosclerotic process but was in all respects similar to the structure of the calcified mitral valves. The calcified nodules appeared to develop in the scar and project outward usually on both surfaces of the valve. The nodules were large enough apparently to impinge in some cases upon the coronary orifices. This may explain the frequent cardiac pain in some of these cases. The cusps were diffusely thickened and their edges were fused. Stenosis to a marked degree was common. The entire process appears to be the end-result of inflammation, probably rheumatic.

Microscopically, the valves showed the presence of an inflammatory reaction or blood vessels or both in nearly all cases. The inflammatory reaction bore no immediate relation to the calcium. The fact that calcium without any proliferative or exudative inflammatory reaction was present in 31 per cent of the cases suggested that the inflammation was not a foreign body reaction to the calcium.

The degree of smoothness in the aorta gave no support to the theory that the thickening of the cusps is due to atherosclerosis. These aortas rather appeared to have been protected by the aortic stenosis and suggested that the valvular disease began early in life.

When the incidence of aortic valvular involvement in cases of acute and recurrent rheumatic endocarditis was compared with the incidence in the group of all old healed valve deformities it was seen that the aortic involvement in the latter was about what should be expected. If the calcified group were not included among the rheumatic healed valve defects there would not be a sufficient number of aortic valve deformities to meet the expectancy. A cause other than rheumatic infection is not necessary to explain the frequency of healed calcified aortic valve disease.

It seems reasonable to conclude that the calcified nodular aortic valve deformity is of common occurrence, that it is the most common healed aortic lesion and that the change in the valves is due to repeated attacks of rheumatic proliferative inflammation with calcification similar to that so commonly seen in the mitral cusps.

SUMMARY

1. The calcified nodular deformity of the aortic valve with stenosis is a clinical type frequently not diagnosed because of the common occurrence of sudden death and the lack of constancy of clinical symptoms and signs and because the clinical symptoms are often similar to other types of heart disease such as coronary sclerosis.

2. This lesion is a common one. It is the usual kind found in healed aortic valve deformities. The healed thickened aortic valves as well as the mitral valves commonly undergo calcification.

3. The available evidences in our material relative to etiology support the rheumatic origin of the lesion rather than the degenerative or atherosclerotic origin.

REFERENCES

1. Christian, H. A.: Aortic Stenosis With Calcification, J. A. M. A. **97**: 158, 1931.
2. McGinn, S., and White, P. D.: Clinical Observations on Aortic Stenosis, Am. J. M. Sc. **188**: 1, 1934.
3. Boas, E. P.: Angina Pectoris and Heart Block as Symptoms of Calcareous Aortic Stenosis, Am. J. M. Sc. **190**: 376, 1935.
4. Contratto, A. W., and Levine, S. A.: Aortic Stenosis With Special Reference to Angina Pectoris and Syncope, Ann. Int. Med. **10**: 1636, 1937.
5. Margolis, H. M., Ziellessen, F. O., and Barnes, A. R.: Calcareous Aortic Valve Disease, Am. Heart J. **6**: 349, 1931.
6. Mönckeberg, J. G.: Der normale histologische Bau und die Sclerose der Aortenklappen, Virchows Arch. f. path. Anat. **176**: 472, 1904.
7. Libman, E.: Some General Considerations Concerning the Affections of the Valves of the Heart, M. Clin. North America **1**: 573, 1917.
8. Ribbert, H.: In Henke, F., and Lubarsch, O.: Handbuch der speziellen pathologischen Anatomie und Histologie, Berlin, Julius Springer **2**: 195, 1924.
9. Geerling, J. G.: Sclerosis annularis valvularum, cited by Soval, A. R., and Gross, L.: Arch. Path. **22**: 477, 1936.
10. Soval, A. R., and Gross, L.: Calcific Sclerosis of the Aortic Valve, Arch. Path. **22**: 477, 1936.
11. Clawson, B. J.: Nonsyphilitic Aortic Valve Deformity, Arch. Path. **12**: 889, 1931.
12. Clawson, B. J., and Bell, E. T.: Valvular Diseases of the Heart, Am. J. Path. **2**: 193, 1926.
13. Cabot, R. C.: Facts on Heart Disease, Philadelphia, 1926, W. B. Saunders Company, p. 206.
14. Marvin, H. M., and Sullivan, A. G.: Clinical Observations Upon Syncope and Sudden Death in Relation to Aortic Stenosis, Am. Heart J. **10**: 705, 1935.
15. Laplace, L. B.: The Relation of Angina Pectoris to Aortic Valvular Disease, Am. Heart J. **8**: 810, 1933.
16. Gross, L.: Significance of Vessels in Human Heart Valves, Am. Heart J. **13**: 275, 1937.

# THE INFLUENCE OF THE SIZE OF CARDIAC INFARCTS UPON THE ELECTROCARDIOGRAM*

HARRY GOLD, M.D., WALTER MODELL, M.D., AND JANET TRAVELL, M.D.
NEW YORK, N. Y.

A VOLUMINOUS literature now exists on the use of the electrocardiogram to determine the location of a clinical cardiac infarct. The types of electrocardiograms produced by the occlusion of the right coronary artery or the left, of infarction located in the right or left ventricle, on the anterior or posterior surface of the heart, or involving one or another of the cardiac muscles, have been explored extensively in experimental and clinical investigations.

The size of the infarction in any location is undoubtedly a matter of considerable prognostic importance. At the present time, the size is inferred chiefly from the severity of the clinical symptoms, it being assumed that severe symptoms of collapse, high fever, cardiac failure, indicate a large infarction, and mild symptoms a small one. Satisfactory information as to the accuracy of this inference does not exist, although it is probably correct in the majority of cases. However, there are several factors which may disturb a parallelism between the severity of symptoms and size of infarction, such as the number of previous occlusions, reflex vasomotor changes, the state of the remainder of the cardiac circulation at the time of an infarction. The extent to which the electrocardiogram can be put to use in judging whether an infarct is large or small has received relatively little attention.

In the hope of throwing some light on this question, we have analyzed the electrocardiographic data from a study in which a large coronary vessel was ligated and the size of the resulting infarct was measured.

## METHOD

The circumflex branch, without the vein, was ligated at its origin from the left coronary artery, in 42 cats. These animals were employed in another study of the effect of aminophylline on the size of a cardiac infarct. Of the entire group, 11 died in from four to seventeen days, and 31 survived longer and were killed three weeks after the ligation. The size of the resulting infarct was measured with a planimeter at the autopsy. For the details of the operative technique, the original

*From the Department of Pharmacology, Cornell University Medical College.

paper may be consulted.[1] Electrocardiograms (3 standard leads) were taken just before the operation, within about ten to thirty minutes after the ligation, the following day, and every third day thereafter.

## RESULTS

The resulting infarction was located on the posterior surface of the heart, involving chiefly the left ventricle. Its circumference was fairly sharply demarcated; its form was irregularly triangular, with its base along the auriculoventricular groove, and its apex extending downward toward the apex of the heart. It showed wide variations in size, from 2.26 to 12.84 sq. cm.

The only electrocardiographic changes that could be correlated with the size of the infarct were the displacement of the R-T or S-T seg-

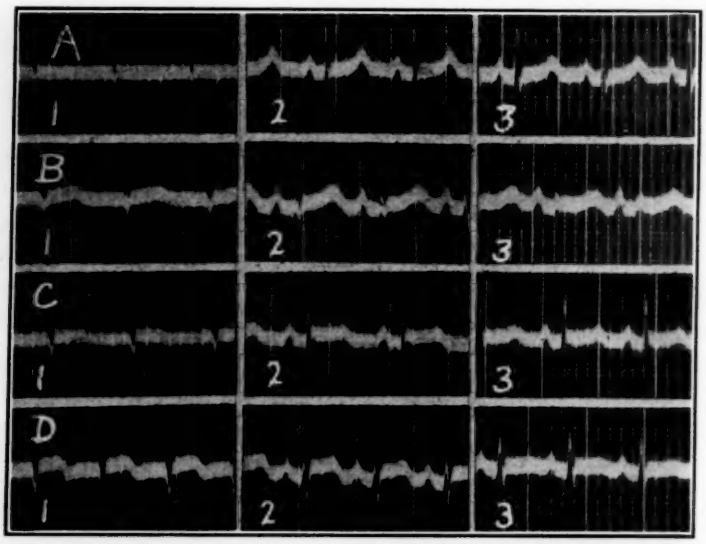


**Fig. 1.—Displacement of R-T or S-T segments due to purulent pericarditis in cat with control operation in which the coronary artery was not ligated. (*A*) Before operation; (*B*) 18 minutes after operation; (*C*) second day; (*D*) seventh day.**

ments, and ventricular tachycardia. Slight displacement of the segments (about 0.5 mm. or less) was sometimes present in the control tracing, and this was taken into account in judging the effects of infarction. Changes in the T-waves were not reliable, as shown by a control series of 13 animals in which the operation was carried through in all its details, except for the ligation of the artery. Electrocardiograms taken immediately after the operation and again at the usual intervals throughout the twenty-one days of study, when compared with the preoperative tracing, showed marked changes in the T-waves and the forms of the QRS groups; a negative T-wave in Leads I or II or both, became isoelectric or positive, and vice versa. The change appeared immediately after the operation, or at some time during the

next thirteen days. In one animal a coupled rhythm, due to premature ventricular contractions, appeared on the twenty-first day. Whether these changes are due to the displacement of the heart as a result of the thoracic operation cannot be stated. It is known that T-wave changes and premature ventricular contractions occur spontaneously in cats.[2] In only two animals did the control operation result in the displacement of the R-T or S-T segment; in one of these on the seventh day, without any apparent explanation at autopsy, in the other apparently on the basis of a purulent pericarditis (Fig. 1).

The results are presented in Table I. Among the 42 animals with a posterior infarct as the result of the ligation of the entire circumflex branch of the left coronary artery 11, or 26.6 per cent, failed to show any displacement of the R-T or S-T segments in the standard three leads of the electrocardiogram. The infarct in the 11 without this change was about one-half to two-thirds as large as in the 31 in which the change was present. In general, also, the more pronounced

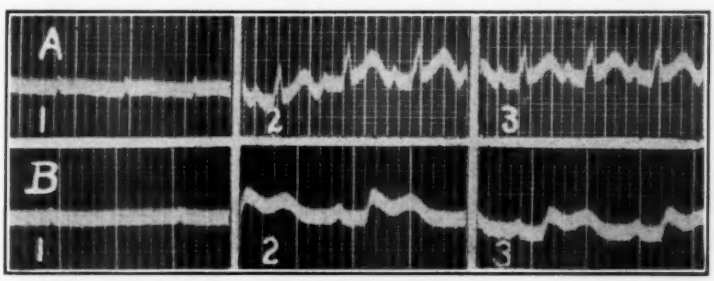


Fig. 2.—Type of R-T change with infarct of average size and with very large infarct. (*A*) Cat 27T. Infarct of average size, 6.97 sq. cm. (*B*) Cat 24T. Very large infarct, 12.84 sq. cm.

changes in the R-T or S-T segment were produced by the larger infarcts. The types of changes produced by the infarcts of average size and by the larger ones are shown in Fig. 2. Individual differences were considerable, however, and, as illustrated in Fig. 3, of two animals having an infarct of the same size, one showed almost no change in the R-T or S-T segment, while in the other, the change was quite marked.

In all animals in which displacement of the segments occurred after the ligation (31, or 73.4 per cent, of the 42 animals), a considerable degree of restitution took place within twenty-four hours, although some displacement was still present at the end of the three-week period in 22 or 71 per cent of the 31 animals in which displacement had occurred. In nine animals in which the R-T segment was restored to normal earlier, the sizes of the infarcts were similar to those in which the change persisted beyond the three-week period, the largest as well as the smallest infarct being represented in this group. The size of

TABLE I

THE RELATION OF THE SIZE OF THE INFARCT TO THE ELECTROCARDIOGRAPHIC CHANGES

| CAT NO. | DISPLACED R-T OR S-T | | 1+ CHANGE | 2+ TO 5+ | VENTRICULAR TACHYCARDIA | RESTITUTION OF DISPLACED R-T OR S-T SEGMENT BEFORE 3 WEEKS |
|---|---|---|---|---|---|---|
| | NO | YES | (0.5 TO 1 MM.) | CHANGE (MORE THAN 1 MM.) | | |
| | (SQ. CM.) | (SQ. CM.) | (SQ. CM.) | (SQ. CM.) | (SQ. CM.) | (SQ. CM.) |
| 1 | | 9.48 | | 9.48 | | |
| 2 | | 7.74 | | 7.74 | | |
| 3 | | 7.36 | | 7.36 | | 7.36 (19)‡ |
| 4 | | 7.29 | | 7.29 | 7.29 (post-operative) | |
| 5 | | 6.97 | | 6.97 | | 6.97 (19) |
| 6 | | 6.32 | 6.32 | | | |
| 7 | 6.07 | | | | | |
| 8 | | 5.94 | | 5.94 | | |
| 9 | 5.61 | | | | | |
| 10 | 4.45 | | | | | |
| 11 | | 4.19 | 4.19 | | | 4.19 (17) |
| 12 | | 3.94 | | 3.94 | | |
| 13 | | 3.74 | 3.74 | | | 3.74 (8) |
| 14 | 3.36 | | | | 3.36 (2)† | |
| 15 | 2.65 | | | | | |
| 16 | 2.58 | | | | | |
| 17 | | 2.26 | 2.26 | | 2.26 (8) | 2.26 (19) |
| 18 (5)* | | 7.36 | | 7.36 | | |
| 19 (9) | | 5.94 | | 5.94 | | |
| 20 (4) | | 5.87 | 5.87 | | | |
| 21 (17) | | 5.48 | | 5.48 | | |
| 22 (11) | | 4.32 | 4.32 | | | |
| 23 (14) | | 2.65 | 2.65 | | | |
| 24T | | 12.84 | | 12.84 | 12.84 (8) | 12.84 (17) |
| 25T | | 9.81 | | 9.81 | | |
| 26T | | 9.10 | 9.10 | | 9.10 (21) | |
| 27T | | 6.97 | | 6.97 | 6.97 (2) | 6.97 (13) |
| 28T | | 6.97 | | 6.97 | | |
| 29T | | 6.90 | | 6.90 | | |
| 30T | | 5.94 | | 5.94 | 5.94 (post-operative) | 5.94 (15) |
| 31T | 5.74 | | | | | |
| 32T | 5.29 | | | | 5.29 (10) | |
| 33T | 3.68 | | | | | |
| 34T | 3.55 | | | | 3.55 (2) | |
| 35T | | 3.23 | 3.23 | | | 3.23 (17) |
| 36T | 3.23 | | | | 3.23 (2) | |
| 37T | | 2.90 | | 2.90 | | |
| 38T (6) | | 9.68 | | 9.68 | | |
| 39T (8) | | 8.39 | | 8.39 | 8.39 (5) | |
| 40T (13) | | 8.00 | | 8.00 | 8.00 (2) | |
| 41T (8) | | 6.45 | | 6.45 | | |
| 42T (8) | | 5.61 | | 5.61 | 5.61 (2) | |
| Total No. | 11 | 31 | 9 | 22 | 13 | 9 |
| Range | 2.58 to 6.07 | 2.26 to 12.84 | 2.26 to 9.10 | 2.90 to 12.84 | 2.26 to 12.84 | 2.26 to 12.84 |
| Average | 4.20 | 6.44 | 4.63 | 7.18 | 6.30 | 5.94 |
| Median | 3.68 | 6.45 | 4.19 | 6.97 | 5.94 | 5.94 |
| Mode | 3.23 to 3.68 | 5.87 to 6.97 | -- | 5.94 to 6.97 | 3.23 to 3.55 | -- |

*Figures in parentheses in this column indicate number of days animal survived the operation.

†Figures in parentheses in this column indicate day after operation when ventricular tachycardia was first seen.

‡Figures in parentheses in this column indicate approximate duration, in days, of displacement of R-T or S-T segment.

(T) Treated with aminophylline 25 mg. per kg., daily, intramuscularly. The treatment was without influence on the size of the infarct, and the two groups were treated as one (1).

the infarct, if it exerts any influence at all, therefore, does not appear to be the sole factor determining the speed of restitution of the displaced R-T segment.

Ventricular tachycardia occurred in 13 animals (31 per cent of the cases), appearing at various times from immediately after the ligation to twenty-one days later. As pointed out in the previous study,[1] the use of aminophylline in many of these might have contributed to the high incidence of ventricular tachycardia. The most frequent size, as well as the average size, of the infarct in those which showed a ventricular tachycardia was essentially the same as in those without it, and the range of infarct sizes in this group covered almost the whole range of infarct sizes in the group without the abnormal rhythm.

In those that were unable to survive the effects of the ligation for as long as three weeks (indicated by the length of survival in the table), the infarct was no larger than in the group that survived longer periods (range of sizes 2.65 to 9.68 sq. cm.; average 6.34; median

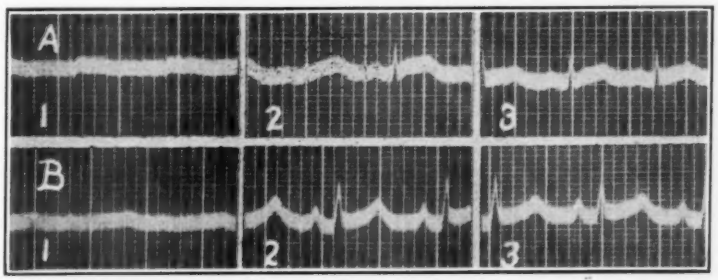


Fig. 3.—Individual differences in R-T changes in case of infarcts of similar size. (*A*) Cat 20; almost negligible displacement; infarct 5.87 sq. cm. (*B*) Cat 8; fairly marked displacement; infarct 5.94 sq. cm.

5.94; mode 5.48 to 5.94). Factors other than the size of the infarct, therefore, play an important rôle in the duration of survival of an even apparently normal animal, after a coronary occlusion. All the 11 animals which failed to survive three weeks developed R-T or S-T displacements, and in 8 of these, the changes were very marked.

## SUMMARY AND CONCLUSIONS

The occlusion of the entire circumflex branch of the left coronary artery (without the vein) in cats caused an infarct of fairly uniform location but of varying size. The electrocardiographic changes were correlated with the different sizes of the infarcts. The results show that: (1) A fairly large proportion (about 25 per cent) may show no R-T or S-T segment displacement. (2) Those which fail, under these circumstances, to develop displacement of the R-T or S-T segments are likely to have the smaller infarcts, and those showing the greatest degree of displacement are likely to have the largest infarcts. (3) Differences in the speed of restitution of the displacement of the R-T or

S-T segment do not indicate differences in the size of the infarcts. (4) The occurrence of ventricular tachycardia throws no light on the size of the infarct, it being present after small as well as after large ones. The ventricular tachycardia therefore appears to depend chiefly upon a focus of irritation rather than upon its size. (5) Individual variations are very marked, and infarcts of the same size may be found in all the groups, among those showing no displacement of the R-T or S-T segments, among those showing slight or marked displacement, among those with, and those without ventricular tachycardia.

REFERENCES

1. Gold, H., Travell, J., and Modell, W.: The Effect of Theophylline With Ethylene Diamine (Aminophylline) on the Course of Cardiac Infarction Following Experimental Coronary Occlusion, AM. HEART J. 14: 284, 1937.
2. Gold, H., Hitzig, W., Gelfand, B., and Glassman, H.: A Qualitative Comparison of Various Digitalis Bodies, AM. HEART J. 6: 237, 1930.

# RESPIRATORY CHANGES PRODUCED IN THE CARDIAC PATIENT BY REBREATHING EXPERIMENTS AS COMPARED WITH THOSE OF THE NORMAL INDIVIDUAL*†

HARRY LANDT, M.D., AND JULIEN E. BENJAMIN, M.D.
CINCINNATI, OHIO

FOR many years workers in the field of experimental medicine have been concerned with devising a method that would quantitatively differentiate, in degree of severity, the cardiac patient from the normal individual. All the muscle exercise tests that have been used suffer from the fact that the individual musculature is a variable which defies quantitation. Furthermore, estimations of change in blood pressure, respiratory rate, and pulse rate are in themselves very gross methods of differentiation. The respiratory rate is not an index of the amount of air handled by the patient.

The fact that the cardiorespiratory system must be considered as a unit is a concept long recognized by the physician. It was the realization of this unity and the belief that the substitution of a progressive anoxemia for muscular exercise would give us a method by which a direct quantitative burden could be placed on the cardiorespiratory system, that led us to investigate the effects of this procedure on the normal and on the cardiac patient.

Our method of investigation was definitely influenced by previous work, the review of which will explain our subsequent approach to the subject. Without delving into the enormous amount of literature dealing with the regulation of the respiratory system, we believe that it can be definitely stated that progressive anoxemia brings into play several compensating mechanisms in the cardiorespiratory function of the body. These compensatory mechanisms are as follows:[1]

A. Progressive anoxemia per se causes increased ventilation of the lungs. More than a decade ago the British Hemoglobin Committee of the Medical Research Conference[2] reported that "the want of oxygen must be regarded as having a direct effect on the respiratory center, and it does not matter whether we regard that effect as due to an actual

*From the Institute for Medical Research of the Jewish Hospital.

†The authors are indebted to Professor Laurence R. Culver of the Engineering Department of the University of Cincinnati for his valuable advice throughout the course of the work. Acknowledgement is also made of the technical assistance of Mr. Nathan Aronoff.

Read before The American Heart Association, section on cardiac disorders, at Atlantic City, N. J., June 8, 1937.

stimulating property of oxygen deficiency or to an increase in the sensitivity of the respiratory center to the hydrogen ion.'' The modern concept of this phenomenon is summarized by Y. Henderson, and Radloff.[3] It is as follows: ''Oxygen deficiency through some nonacidotic process increases the sensitivity of the respiratory center to its specific stimulus; the hydrogen ion concentration of the blood plasma.'' Schneider[4] has also shown that in rebreathing experiments, when the oxygen is depleted and the carbon dioxide is filtered out, the depth of

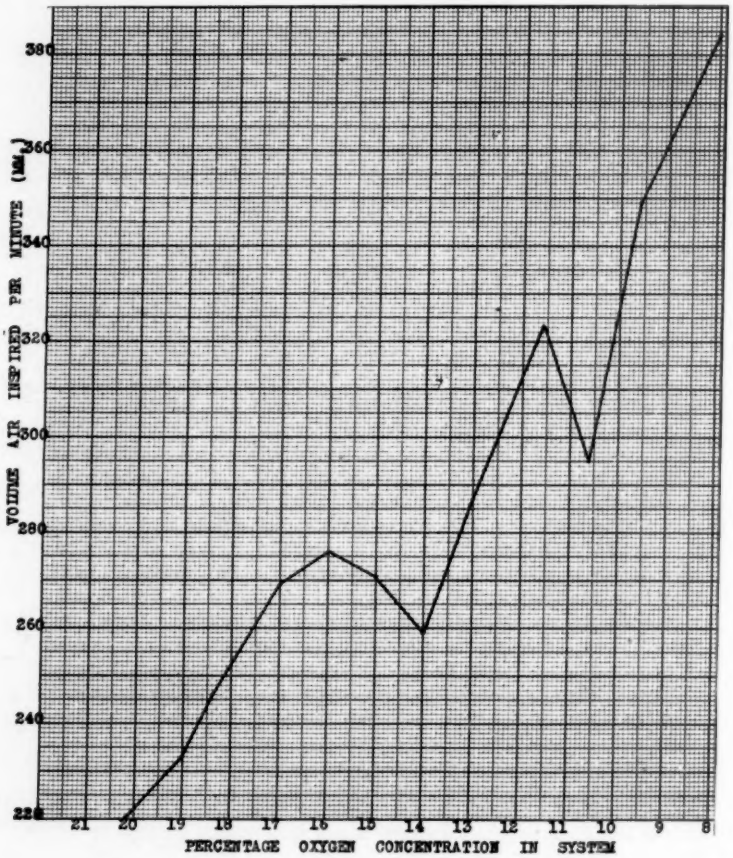


Fig. 1.—M. R., aged twenty-four years (normal).

the respirations tends to increase rather than the rate. Thus we see the effect of anoxemia on the respiratory system per se.

B. The second compensatory mechanism, according to Wiggers,[1] is brought about by the resultant hyperpnea which has the value of elevating the blood oxygen tension. This is accomplished by a greater admixture of the air in the spirometer with the alveolar air. In addition to this there is evidence which points to the opening of previously unused or partially used alveolar spaces, thus allowing for a better

equilibrium between the alveolar and the blood gases. However, because of the decreased dissociation of oxyhemoglobin in the associated hypocapnic state the benefit of the hyperpnea is considerably less than may be inferred.

C. The third compensatory mechanism,[1] namely the increase in the number of circulating red cells which occurs as the result of anoxemia, cannot be of as great importance as one might infer. True, more oxygen

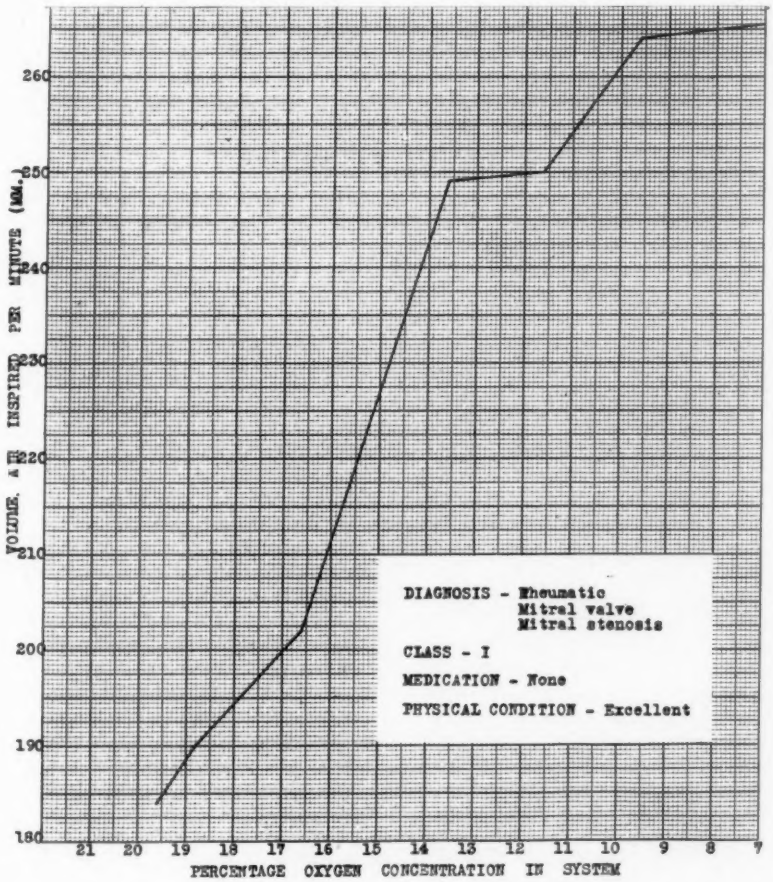


Fig. 2.—V. A., aged eighteen years (cardiac).

is carried to the capillaries as a result of this mechanism, but we must bear in mind that it is the partial pressure of this gas that is of the greatest importance. Haldane and Barcroft[5] state that the increased volume of the transported oxygen may keep the partial pressure of the gas from falling as rapidly as it might otherwise do.

D. The fourth compensatory mechanism[6] is that of increased cardiac output. Recent studies have shown that the cardiac rate is accelerated and the heart forces are increased when the oxygen reaches about 14 per

cent. These reactions are greatly increased when the oxygen reaches 12 per cent or 11.5 per cent. Furthermore, the diastolic size of the heart increases and the muscle output is augmented.[7] In addition to this the arterial pressures rise and the pulse pressure tends to become greater.[7] Wiggers suggests that this mechanism accomplishes what the three other mechanisms accomplish imperfectly.

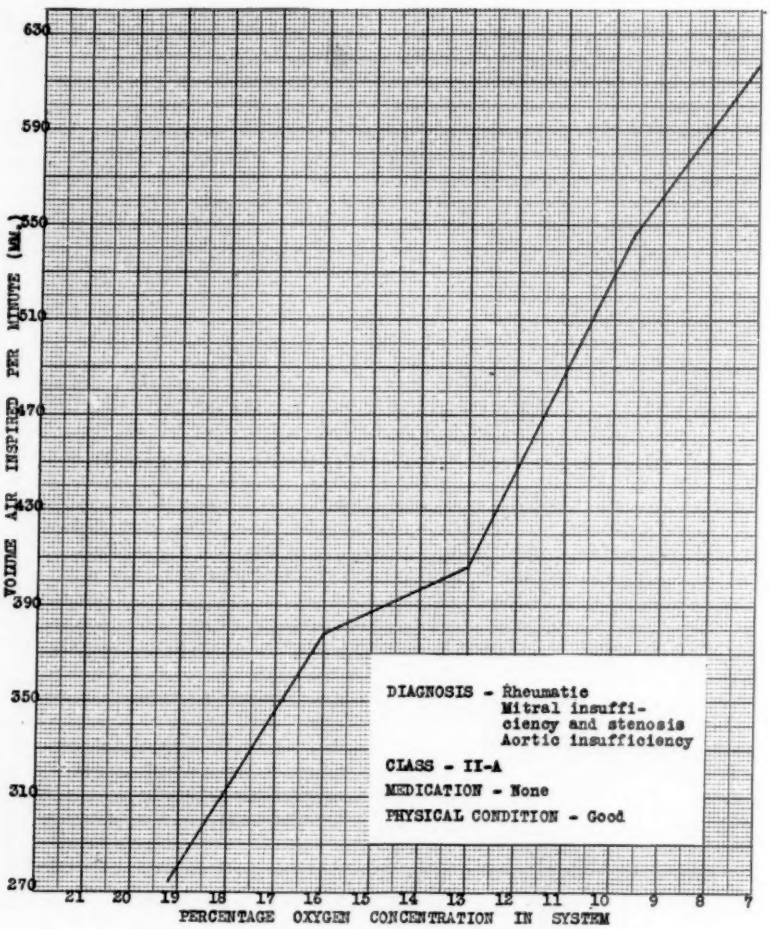


Fig. 3.—W. F., aged twenty-two years (cardiac).

As a result of the observations just quoted it was our premise that the cardiorespiratory system of the cardiac patient could not respond with the facility of that of the normal individual when subjected to decrease in oxygen concentration. Therefore, progressive anoxemia, which could be measured, was employed as the method of producing a burden on the cardiorespiratory system. To accomplish this, atmospheric air was used in a rebreathing apparatus fitted with a $CO_2$ filter and progressive anoxemia was produced by the patient's utilization of the oxygen in this system.

## METHOD

The patient was prepared for the test in the manner used when a basal metabolic rate is taken. A calibrated McKesson spirometer with a specially constructed flowmeter was employed. All tests were started with ten liters of air in the spirometer. In order to prolong the test a continuous flow of 50 c.c. of oxygen per minute was allowed to filter into the system, care being taken to place the oxygen inlet at the opposite side of the tank from the air outlet. The spirometer was fitted with a

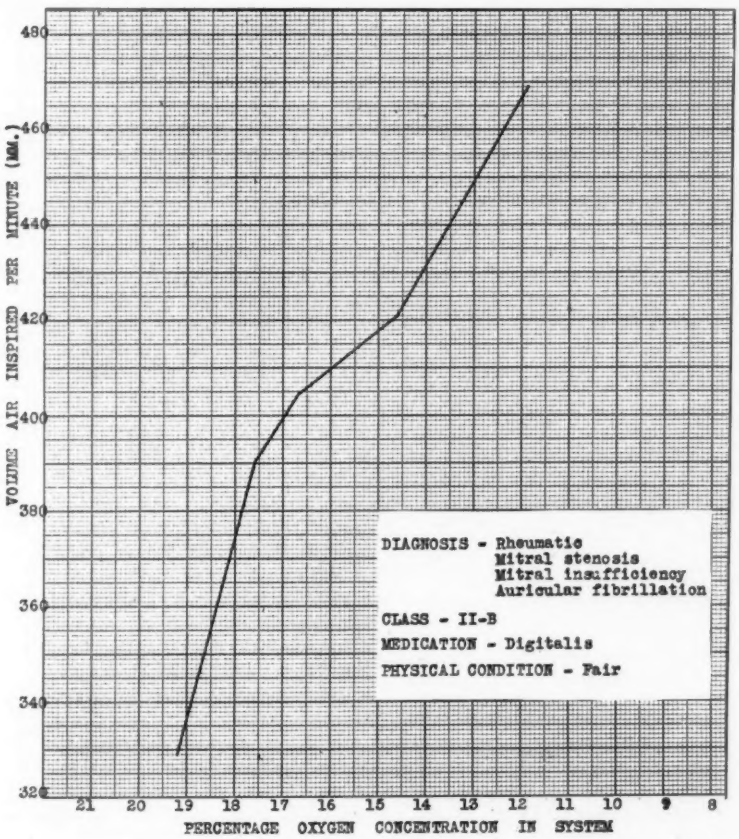


Fig. 4.—H. W., aged thirty-one years (cardiac).

double speed motor which spread out the graph and allowed for more accurate measurements. In all, forty normal and forty cardiac patients, including Class I, Class II-A, and Class II-B types, were tested several times. Representative results are graphically illustrated in the accompanying charts.

## DISCUSSION AND RESULTS

It will be noted from the graphs that in the normal patient there is a definite decrease in the amount of air respired between the range of 16 per cent to 13 per cent, and about 12 per cent to 11.5 per cent oxy-

gen concentration, yet oxygen depletion of the system continues. From previously quoted work it will be noted that it is in this range that the cardiac output increases. The charts of the cardiac patients do not show this decrease in volume respiration. The cardiac group in Class I tend to show a leveling off in the 16 per cent to 13 per cent oxygen range but in no instance did a downward slope in the curve occur. The other cardiac patients in Class II-A and Class II-B, respectively, show either a curve which has a slight tendency to level off or a continued sustained elevation in the curve of the graph.

From our observations it appears that at certain stages the respiratory system must function with a facility inversely proportional to the ability of the heart to increase its load. At present we are unable to state the attending chemical changes occurring in the body during this procedure. There is the definite possibility that these curves may lend themselves to corrections for surface area and individual minute oxygen consumption, but we have reason to believe that these corrections are immaterial. We feel that this method takes into account important factors, not given adequate consideration in the past. Furthermore, it eliminates the variables inherent in the previous methods.

## CONCLUSIONS

1. Normal individuals respond to anoxemia differently from cardiac patients.

2. The difference consists in the ability of the heart to compensate for the burden produced by anoxemia.

3. The burden placed on the cardiorespiratory system can be quantitated.

4. The curve of response to the burden seems likewise to be quantitative.

## REFERENCES

1. Wiggers, Carl J.: Physiology in Health and Disease, Philadelphia, 1934, Lea & Febiger, p. 398.
2. Idem: Ibid., p. 393.
3. Henderson, Y., and Radloff, E. M.: Am. J. of Physiol. **101:** 647, 1932.
4. Schneider, E. C.: Physiological Review **1:** 631, 1921.
5. Haldane, and Barcroft: 1925—Quoted by Wiggers, Carl J. Physiology in Health and Disease, p. 399, 1934.
6. Wiggers, Carl J.: Physiology in Health and Disease, p. 399, 1934.
7. Sands and DeGraff: Am. J. Physiol. **74:** 416, 1925; Harrison, et al.: Ibid. **80:** 169, 1927; **83:** 275, 1927; Gollwitzer-Meier: Pflüger's Arch. f. d. ges. Physiol. **220:** 434, 1928; Grollman: Am. J. Physiol. **93:** 19, 1930; Strugold: Ibid. **94:** 641, 1930.

# ELECTROCARDIOGRAPHIC CHANGES FOLLOWING THE INHALATION OF TOBACCO SMOKE*

ASHTON GRAYBIEL, M.D., BOSTON, MASS., ROBERT S. STARR, M.D., HARTFORD, CONN., AND PAUL D. WHITE, M.D., BOSTON, MASS.

IT HAS long been known that tobacco or nicotine may cause changes in cardiac activity. Traube,[1] in 1862, while studying the action of nicotine on the dog's heart observed that there is at first a slowing or even temporary cardiac arrest followed by tachycardia with reinforced contractions. Since that time there have been a great many experiments showing that tobacco or nicotine may alter cardiac activity and may provoke various auricular and ventricular arrhythmias and auriculoventricular block of all grades.

Bull, Clerc, and Pezzi,[2] in 1914, were among the first to use the electrocardiograph in studying the effects of nicotine on the heart. They took electrocardiograms on dogs and rabbits which had been injected with toxic doses of nicotine and observed nodal rhythm, auricular flutter, and heart-block. These observations have been repeatedly confirmed and recently extended by Mattioli[3] who studied the electrocardiographic changes in rabbits following acute and chronic tobacco poisoning and acute nicotine poisoning; the changes were similar in all experiments and consisted chiefly of partial heart-block, increase in amplitude of the T-waves, and decrease in amplitude of the R-waves.

Ssalischtscheff and Tschernogoroff[4, 5] were the first to study the effect of the inhalation of tobacco smoke on the human electrocardiogram. They asked healthy individuals to smoke until toxic symptoms appeared and electrocardiograms were taken every five to ten minutes during the test. Arrhythmias and heart-block were not observed and characteristic alterations in the form and amplitude of the several waves were not found save in two instances where there was slight lowering of the T-waves. The heart rate was accelerated in each instance save one where the rate slowed from 75 to 52 a minute.

Our interest in the effect of tobacco on the electrocardiogram was stimulated by observations on a healthy young man of eighteen years who complained of dizziness on smoking. Electrocardiograms taken after the inhalation of tobacco smoke showed well marked inversion of the T-waves in Leads II and III while at other times the T-waves were upright and of normal amplitude. To determine whether or not this is a common phenomenon similar tests have been carried out on 45 individuals.

*Presented in brief before the New England Heart Association, Massachusetts General Hospital, Boston, Nov. 9, 1936.

*Method.*—The subject to be tested was asked not to smoke for at least one hour preceding the test. After resting comfortably in a chair or bed until the blood pressure and pulse rate reached steady values a control electrocardiogram was taken. The smoke of a cigarette was then inhaled until either toxic symptoms appeared or the cigarette was finished. Electrocardiograms, and blood pressure and pulse rate determinations were taken repeatedly and notes were made of significant signs and symptoms. In order to allow comparison between the several tracings standardization of the electrocardiograms was carefully done and care was taken that the subject did not shift the position of the body during the course of the experiment. The procedure varied somewhat in that occasionally a pipe or cigar was smoked rather than a cigarette, and sometimes two or three cigarettes were smoked consecutively. In some instances cubebs were smoked as a control and sometimes the effect of atropine was noted.

*Data.*—Among the 45 subjects tested there were 3 women. The ages of individuals in the group varied between eighteen and sixty-four years. Four were nonsmokers, 4 smoked occasionally, and 37 were confirmed tobacco addicts. Sixteen gave a history of symptoms on smoking, chiefly dizziness, palpitation, and nausea. Two had hypertensive, 8 coronary, and 1 hypertensive and coronary heart disease. During the test 28 complained of cerebral, cardiac, or gastrointestinal symptoms.

The temporary increases in heart rate and in blood pressure following the use of tobacco are well known. Thirty-nine of the 45 showed an increase in heart rate which averaged 13 a minute, 4 a decrease which averaged 15, and 2 no change. Twenty-four of 31 tested exhibited an increase in arterial blood pressure which averaged 13 mm. Hg systolic and 7 mm. diastolic; 6 showed a decrease averaging 13 mm. systolic and 3 mm. diastolic; 1 showed no change.

Twenty of the 45 tested showed significant electrocardiographic changes other than variation in heart rate. Of the 20, 2 were nonsmokers, 1 smoked occasionally, and 17 were heavy smokers; 10 of the 20 gave a history of symptoms on smoking and 15 had symptoms while the test was being done.

The commonest electrocardiographic change was a decrease of from 1 to 4.5 mm. in amplitude of the T-waves in Lead I or II which was observed in 15 instances. In two instances there was an increase in the amplitude of T in Lead I or II. A slight decrease in the length of the P-R interval was observed twice, both times associated with fast heart rates. In two instances the P-R interval was increased, once from 0.16 second to 0.22 second. There was a decrease of 20 per cent or more in the amplitude of the QRS complexes in 4 instances and an increase in one other.

The T-wave changes are of especial interest. Fig. 1 shows electrocardiograms taken on a healthy young man aged eighteen years who

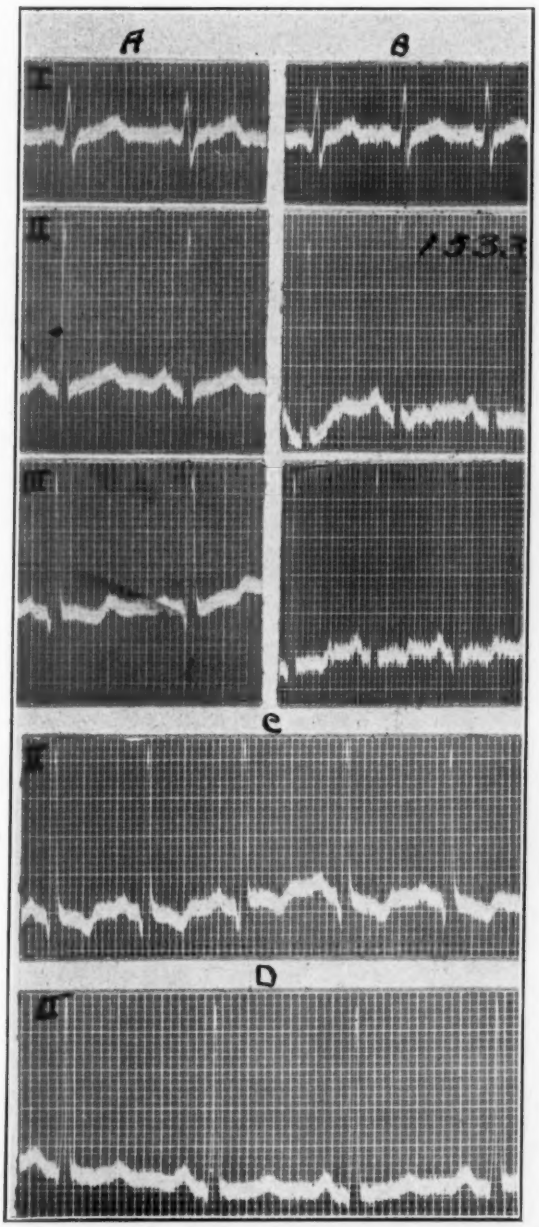


**Fig. 1.—Electrocardiograms taken on a healthy young man, aged eighteen years. *A*, control; heart rate 85. *B*, immediately after smoking; rate about 100. *C*, Lead II taken thirty seconds after *B*; rate about 100. The Q-wave is more prominent in this strip but there is no doubt that it is Lead II. *D*, Lead II (a continuation of *C*) taken one minute later.**

complained of dizziness on smoking cigarettes. *A* is the control and *B* the electrocardiogram taken immediately after smoking; note the decrease in the height of T in Leads II and III. *C* is a strip of Lead II taken about thirty seconds after *B;* note the well-marked inversion of T. *D* was taken a minute later; the T-waves are again upright. The test was repeated on another occasion with similar results. Unfortunately the subject was not available for further tests.

The electrocardiograms in Fig. 2 were taken on a healthy woman aged twenty-six years. *A* is the control and *B* the electrocardiogram taken after she finished smoking a cigarette. She complained of dizziness and slight nausea. There is marked lowering of the T-waves in Leads I and II, decrease in amplitude of the QRS complexes, increase in prominence

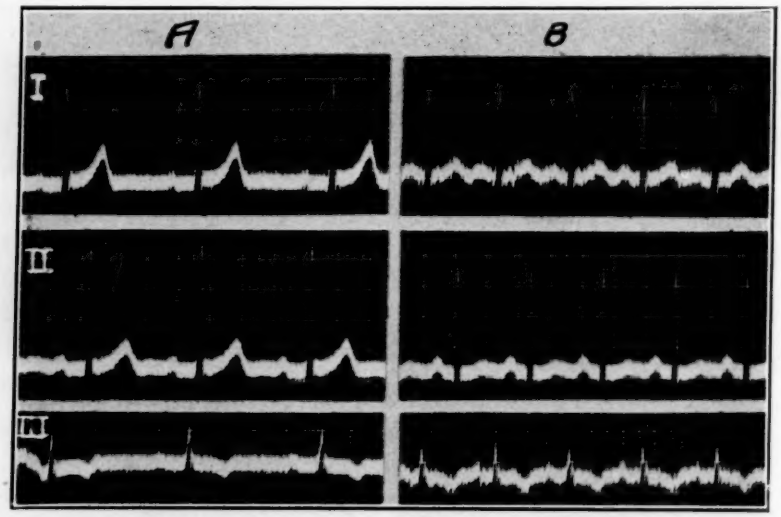


Fig. 2.—Electrocardiograms from a healthy woman, aged twenty-six years. *A*, control; heart rate 80, blood pressure 110/75. *B*, after smoking; heart rate 130; blood pressure 120/90.

of the P-waves, and a slight decrease in the P-R interval. The electrocardiograms in Fig. 3 were taken on the same individual. *A* is the control tracing. *B* was taken ten minutes after 0.002 gm. of atropine sulfate was given intravenously; note especially the decrease in the height of the T-waves in Leads I and II. *C* was taken immediately after the inhalation of cigarette smoke and ten minutes after *B;* the amplitude of the T-waves in Lead II has increased. *D* was taken two minutes after *C;* the T-waves are now comparable to those in *B*.

The electrocardiograms in Fig. 4 were taken in the case of a healthy woman aged twenty-four years. *A* is the control electrocardiogram, *B* was taken after the smoking of one cigarette, and *C* after the smoking of a second cigarette. At this time she was pale, and complained of slight dizziness. Note the decrease in amplitude of the T-waves in all

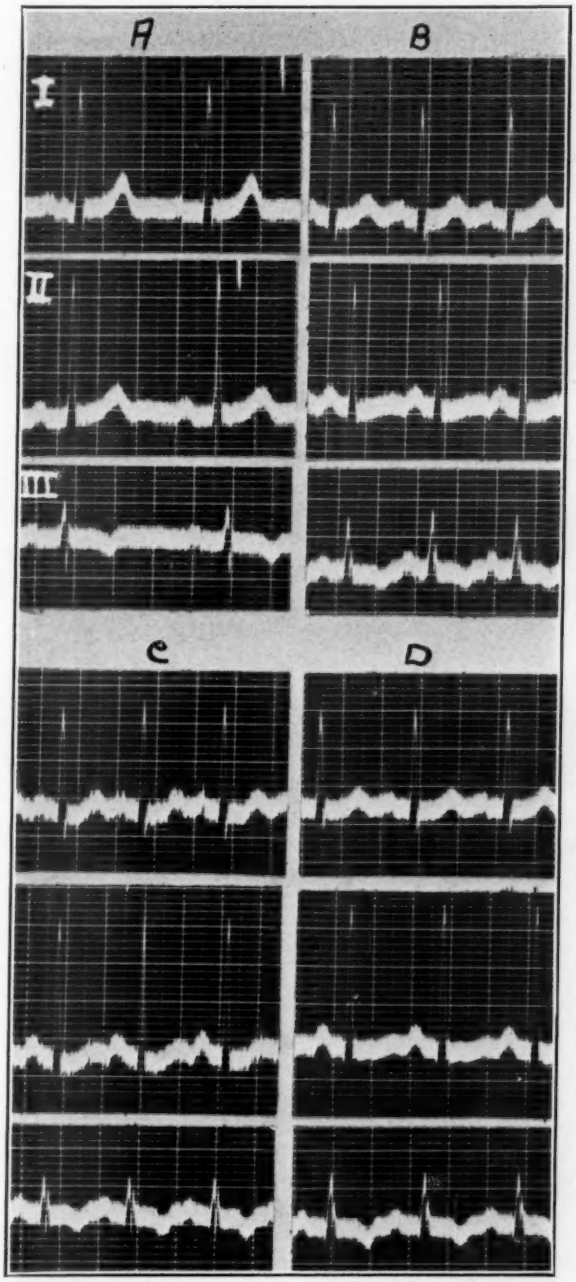


Fig. 3.—Electrocardiograms from a woman, aged twenty-six years. *A*, control; heart rate 85, blood pressure 120/75. *B*, after 0.002 gm. atropine intravenously; rate 130; blood pressure 120/90. *C*, taken immediately after smoking; rate 130, blood pressure 120/95. *D*, taken two minutes later; rate 125, blood pressure 110/85.

leads. *D* was taken four minutes after *C*. The electrocardiograms in Fig. 5 were taken on the same individual. *A* is the control and *B* was taken two minutes after the intravenous injection of 0.002 gm. atropine

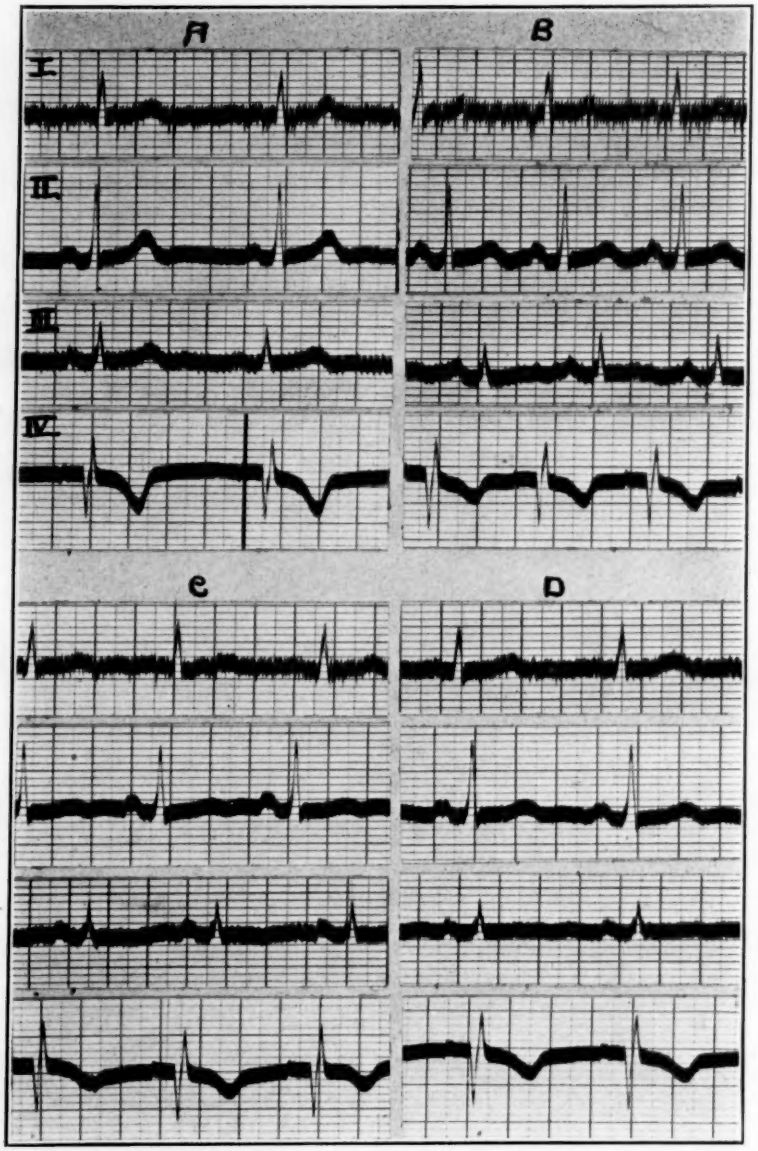


**Fig. 4.**—Electrocardiograms from a woman, aged twenty-four years. *A*, control; heart rate 65, blood pressure 100/70. *B*, after one cigarette; rate 90, blood pressure 125/85. *C*, after a second cigarette; rate 85 to 90. *D* was taken four minutes after *C*; rate 75, blood pressure 110/70. (Lead IV was taken with the electrode from the right arm placed on the chest.)

sulfate. *C* was taken two and D forty-six minutes later. Note especially the flattening of the T-waves in *C*.

Six individuals were tested with adequate doses of atropine as well as with tobacco smoke. In two individuals neither atropine nor tobacco caused a significant change in the T-waves, in two others both drugs caused a moderate decrease in the amplitude of the T-waves and in the

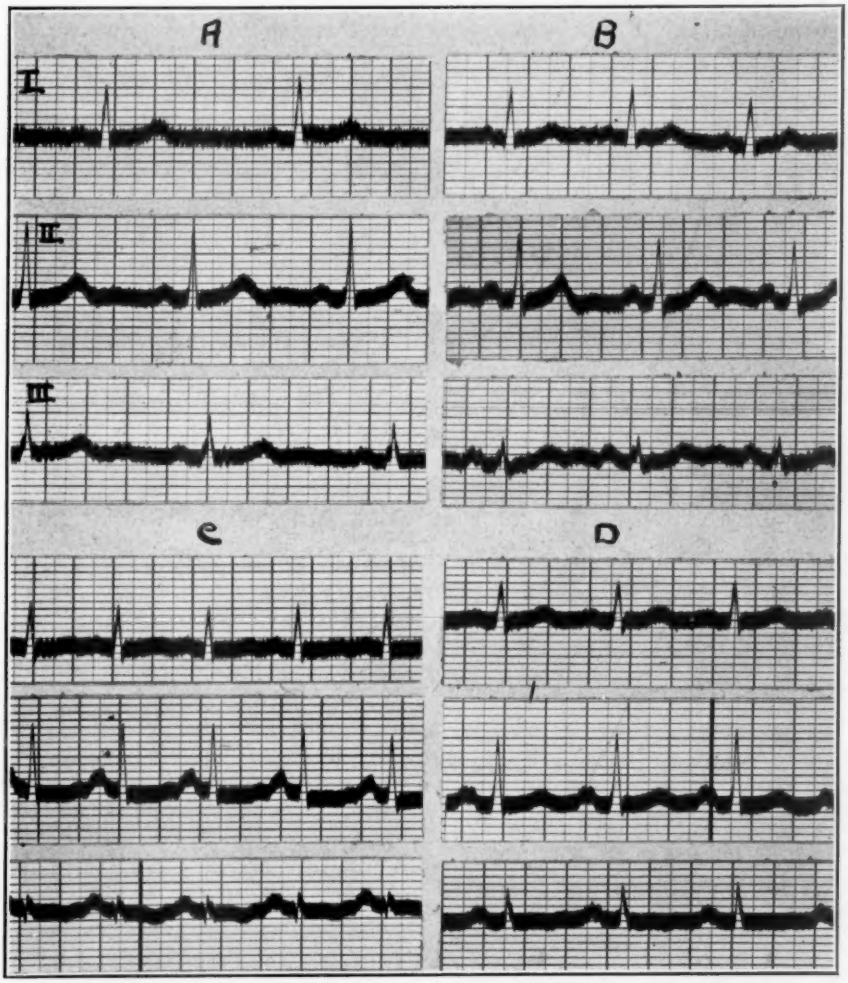


Fig. 5.—Electrocardiograms from a woman, aged twenty-four years. *A*, control; heart rate 65, blood pressure 100/72. *B*, taken two minutes after 0.002 gm. atropine; rate 90. *C*, four minutes after atropine; rate 130, blood pressure 102/78. *D*, forty-six minutes after atropine, rate 105.

remaining two, both drugs caused a marked lowering of the T-waves. Thus in each instance the effects of atropine and of smoking on the T-waves were similar.

## DISCUSSION

It is interesting to consider how the inhalation of tobacco smoke might influence the electrocardiogram.

When tobacco is smoked the chief poisons carried over are pyridine bases, carbon monoxide, and nicotine. The pyridine compounds are irritating to the mucous surfaces but the amounts absorbed are too small to be of toxicological interest.

A carbon monoxide saturation of the hemoglobin as high as 8 per cent has been shown to occur after smoking but usually the saturation is not over 3 or 4 per cent. It is extremely unlikely that this amount is ordinarily injurious, as the healthy individual does not, in most cases, exhibit symptoms until the hemoglobin saturation reaches 15 to 20 per cent. Exceptionally an individual may be extremely sensitive to this gas and notices mild symptoms with concentrations such as may result from smoking. Although it has been shown that significant inversion of the T-waves of the electrocardiogram may result from carbon monoxide poisoning this is highly unlikely under the circumstances considered here.

The poison most seriously to be considered is nicotine. The cigarette chiefly used in these tests contains about one gram of tobacco which, analysis has shown, yields 2.52 per cent nicotine. The smoke from about two-thirds of the cigarette may be inhaled if allowance is made for the stump and the amount burned with the cigarette out of the mouth. If the cigarette is smoked in a period of five minutes, at least one-half of the nicotine will carry over in the smoke and of this at least one-fourth will be absorbed into the system. Consequently somewhere in the neighborhood of 2.0 mg. of nicotine will be taken into the circulation. This amount is sufficient to produce its characteristic action which is stimulation of the entire nervous system followed by depression.

The chief effects upon the heart and vessels of stimulation or paralysis of the vagus and sympathetic nerves are well known. The action of nicotine on these nerves or their ganglia offers an adequate explanation for the changes in pulse rate and blood pressures observed during smoking. Whether or not the same explanation holds true for the T-wave changes is problematical. Many observers have shown that stimulation of the sympathetic nerves or the injection of adrenin causes an increase in amplitude of the T-waves while stimulation of the vagus nerves or the injection of acetylcholine causes a decrease in their amplitude. In man, paralysis of the vagus nerves with atropine is usually regarded as having little or no effect on the T-waves.

In a susceptible individual the initial lowering of the T-waves occurs during the inhalation of the tobacco smoke but the maximum lowering or even inversion of T occurs shortly after smoking ends. The inversion or flattening of T lasts only a few minutes and within half an hour the T-waves assume their normal form and amplitude. If a second cigarette is smoked while the T-waves are still flattened as a result of the first, the T-waves may temporarily increase in amplitude due presumably to sympathetic stimulation. This increase in amplitude

is quickly followed by a decrease and the T-waves may become lower than before. This temporary increase in T may also be seen (Fig. 3) when a cigarette is smoked during full atropinization which has flattened the T-waves. Here again it is probably due to sympathetic stimulation. We were surprised to find that the T-wave changes after full atropinization and after smoking were strikingly similar. Actually the

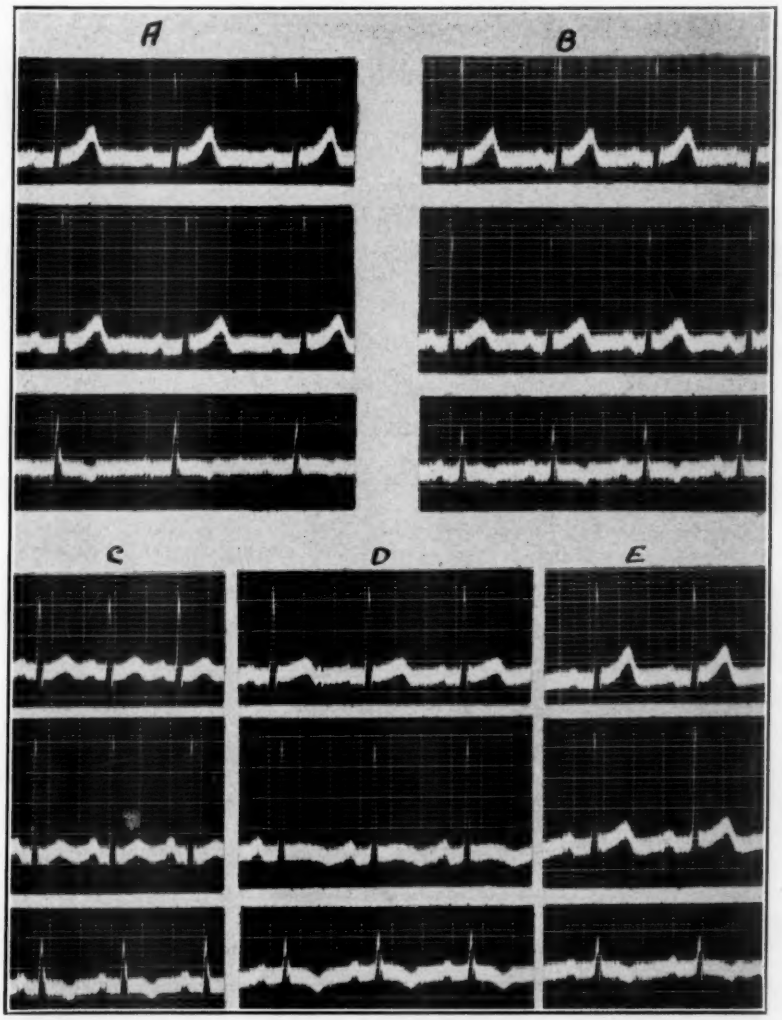


Fig. 6.—Electrocardiograms in the case of a healthy woman, aged twenty-six years. *A*, control; heart rate 80. *B*, taken twenty-three minutes after 1.3 mg. atropine, subcutaneously, rate 92. *C*, taken during smoking; rate about 120. *D*, taken eight minutes after smoking; rate about 100. *E*, taken thirty-six minutes after smoking.

effect of one drug may be used to predict the effect of the other. The individuals showing marked lowering or inversion of the T-waves with tobacco and with atropine were in each instance young and healthy but emotionally labile. More stolid individuals, even those with severe coronary arteriosclerotic heart disease did not show these T changes.

It is interesting that Cohn, Fraser, and Jamieson,[6] who found that atropine alone produced no effect on the T-waves, did find that this drug brought on or intensified the characteristic modification (lowering or inversion) of the T-waves seen during digitalization. White and Sattler[7] and Favill and White[8] also observed that atropine increased the digitalis effect on the T-wave while exercise had the opposite effect. We have observed this same synergistic effect with atropine and nicotine in susceptible individuals but only when atropine was given in amounts insufficient to produce its characteristic effect alone (Fig. 6).

Undoubtedly a few individuals are peculiarly susceptible to the small amounts of nicotine absorbed during smoking. So far as the cardiac effects of this amount of nicotine are concerned its action suggests chiefly parasympathetic paralysis and sympathetic stimulation. Some proof that parasympathetic paralysis may account for the flattening or inversion of the T-waves is afforded by the similar flattening following atropine. Both drugs cause an increase in heart rate but no lowering of blood pressure.

Although it is possible that nicotine may cause the T-wave changes by its action on the heart muscle fibers, there is no reason to believe that myocardial ischemia is a factor. These changes occurred most strikingly in young healthy individuals, anginal pain was never present during the tests, and amyl nitrite failed to influence the T-wave changes following both nicotine and atropine. Furthermore, Laubry and his coworkers[9] have shown that tobacco or nicotine in small amounts actually increases the coronary flow in the isolated rabbit's heart and that toxic doses are necessary to produce vasoconstriction.

There have been reported and we have observed,* attacks of angina pectoris following smoking in patients with small coronary reserve. The explanation commonly offered is that the attacks are the result of coronary vasoconstriction. However, the true explanation, in some instances at least and probably in most, is the sudden increase in work of the heart. This is shown by a striking increase in heart rate, or blood pressure or both. It is this extra work suddenly placed on the heart that is responsible for the precipitation or aggravation of angina pectoris in patients with little heart reserve and unusual sensitivity to tobacco smoke.

## SUMMARY AND CONCLUSIONS

1. We have made observations on 45 individuals of varying ages, some with heart disease, during the inhalation of tobacco smoke.

2. It has long been known that tobacco or nicotine may be responsible for temporary symptoms referable not only to the cardiovascular system but other systems as well. Thirty-nine of the 45 patients in this series

*These observations will be reported later in detail.

exhibited on smoking an increase in heart rate which averaged 13 a minute; 24 of 31 tested showed an increase in arterial blood pressure which averaged 13 mm. Hg systolic and 7 mm. diastolic.

3. Of particular interest were certain electrocardiographic changes, especially lowering or inversion of the T-waves, which occurred during the test in 15 individuals.

4. The probable explanation for the T-wave changes lies in the characteristic action of nicotine on the cardiac ganglia. Actually the T-wave changes following smoking were found to be similar to those following atropinization.

5. It is suggested that in those occasional instances where attacks of angina pectoris are precipitated by smoking ("tobacco angina") the attacks are not the result of coronary vasoconstriction but the result of a sudden increase in the work of the heart as shown by the increase in blood pressure, or heart rate or both.

## REFERENCES

1. Traube: Versuche über den Einfluss des Nicotins auf die Herzthätigkeit, Allgem. med. cent. Zeit. **31**: 281, 1862.
2. Bull, Clerc, and Pezzi: Recherches Électrocardiographiques sur l'action de la nicotine, Soc. Biol. **77**: 213, 1914.
3. Mattioli, M.: Variazione elettrocardiografische nel tabagismo e nel nicotinismo, Morgagni **74**: 59, 1932.
4. Ssalischtscheff, A. S., and Tschernogoroff, J. A.: Elektrokardiographische Analyse der Nicotinwirkung auf das Herz, Ztschr. f. d. ges. exper. Med. **64**: 319, 1929.
5. Idem: Weitere Beobachtungen über die Veränderungen im Elektrokardiogramm und im Sphygmogramm beim Menschen unter den einfluss der Stoffe des Tabakrauches, Ibid. **78**: 193, 1931.
6. Cohn, A. E., Fraser, F. R., and Jamieson, R. A.: The Influence of Digitalis on the T-wave of the Human Electrocardiogram, J. Exper. Med. **21**: 593, 1915.
7. White, P. D., and Sattler, R. R.: The Effect of Digitalis on the Normal Human Electrocardiogram, With Especial Reference to A-V Conduction, J. Exper. Med. **23**: 613, 1916.
8. Favill, J., and White, P. D.: Voluntary Acceleration of the Rate of the Heart Beat, Heart **6**: 175, 1915-17.
9. Laubry, C., Walser, J., and Deglaude, L.: Action expérimentale du tabac et de la nicotine sur le debit coronarien, Bull. Acad. de méd. Paris **109**: 595, 1933.

# ELECTRICAL ALTERNANS OCCURRING IN A CASE WITH PERICARDIAL EFFUSION*

L. Feldman, M.D.
Chicago, Ill.

ELECTRICAL alternans consists of a regular alternation at equal intervals in amplitude or contour, or both, of various phases of the electrocardiographic tracing. In frequency, it is in sharp contrast to the usual and well-known type of alternans which is confined to the pulse or apex beat, but not registered on the electrocardiogram. Electrical alternans, like pulsus alternans, is a sign of reduced myocardial power, yet the electrocardiogram only rarely demonstrates it.[1] In a series of 6,000 electrocardiograms at the Cardiac Clinic of the University of Illinois, not one instance of electrical alternans was encountered.

The most frequent forms are those involving the T alone or both the QRS and T-waves, while alternation of the P-waves alone is one of the rarest forms as described by Chini.[2] Alternation in the auriculoventricular and intraventricular conduction in man has recently been observed.[3, 4] Electrical alternans may vary in degree; it may be continuous, but more often is transient,[4, 5] a fact which may account for its rarity. It is of less significance when seen in extreme tachycardia[6] or following premature contractions.[7]

Mines[8] in 1913 was first to describe isolated electrical alternans in the electrocardiogram obtained from the frog's heart. A number of papers dealing with the experimental and the clinical side of electrical alternans have followed, especially in the foreign literature: Condorelli,[9] Galata,[10] Pezzi[11] and Chini[12] have called attention to this phenomenon during the last decade. Bruno Kisch[13] considers alternation as an expression of the mechanical behavior of the ventricles. He believes that all types of alternans are expressions of a basic alternans of the heart, "herzalternans." According to him, this phenomenon may in various instances be demonstrated best by the electrocardiogram, by the pulse curve, or by other methods of examination. Katz[14] states, "We feel that electrical alternans has the same significance, at a slow rate particularly, as pulsus alternans."

Hamburger, Katz, and Saphir[4] were the first in this country to describe two cases of electrical alternans without pulsus alternans. In the experience of these authors, the combination of mechanical and electrical alternans is rare, while isolated electrical alternans without apparent

*From the Department of Medicine, University of Illinois, College of Medicine, and the Mount Sinai Hospital.

mechanical alternation they considered most unusual. In one case the alternans was a discordant one of the QRS and T-waves. In the second the alternation involved the QRS only. They also cite a case, displaying alternation of the auriculoventricular conduction only. In their first case autopsy revealed an anomalous distribution of the right coronary artery, narrowing of the mouth of this artery, generalized coronary sclerosis, and multiple microscopic myocardial infarcts. In the second case, multiple minute carcinomatous metastases within the myocardium and in the blood vessels of the heart were found post mortem. They concluded that malnourishment of fractions of the heart was responsible for the electrical alternation.

Missal and Crain[3] recently reported a case with bundle-branch block displaying alternation in the intraventricular conduction and T-waves. There were cycles showing a decrease of the width of the QRS from 0.13-0.10, followed by T-waves which became inverted. This phenomenon was observed in the absence of premature contractions, and respiratory excursion did not have any relationship to this unique alternation. They suspected the patient's hyperactive carotid sinus to be causal, although at no time did they succeed in producing this alternation by stimulating the carotid sinus, even to the point of convulsions.

Brody and Rossman[5] just recently have reported two additional cases of electrical alternans, one with pulsus alternans and one without. The first case suffered from degenerative heart disease. The alternation involved the QRS deflections only and was transient. An arteriogram taken at the time when the alternans was absent, showed no mechanical alternation. The second case had rheumatic heart disease and was thirty-nine years old. The alternans was confined to the QRS complexes. She subsequently developed auricular fibrillation.

Another case of electrical alternans with autopsy findings is added to the literature, occurring in a patient with pericardial effusion, resulting from carcinomatous metastasis to the pericardium. The electrocardiogram was encountered after the patient's death, hence the absence of a clinical study of the pulse for mechanical alternation.

## REPORT OF CASE

Mrs. G., fifty-four years of age, married, and a housewife, was admitted to the orthopedic service of the Mount Sinai Hospital on April 19, 1936. Three months before admission she began to suffer from "arthritic" pains affecting her spine, shoulders, and hips. She also knew of an existing hypertension which was symptomless, except for an occasional dizzy spell. Three weeks before entry, while undergoing hot pack treatment for her "arthritis," she suddenly became dyspneic, experiencing substernal pressure, but no actual pain. Since that time, besides pains around and in the joints, she had had substernal discomfort, with choking sensation when lying down. There was some cough, which at times would cause slight pain in the left axilla. There had been some loss of weight in the last four months.

Her previous history revealed the removal of the left ovary and tumor of breast, ten and eight years ago respectively. There had been multiple pregnancies.

The medical consultant found a fairly obese woman, face pale, who could not lie down. Her temperature was 99.8° F.; pulse, 120 and regular; and blood pressure, 148/100. The veins of the neck were not distended. The heart extended about 13 cm. to the left and 4 cm. to the right of the midsternal line. There was appreciable retromanubrial dullness. The heart sounds were clear, but distant. No rubs were heard and there was evidence of fluid in the left pleural cavity,

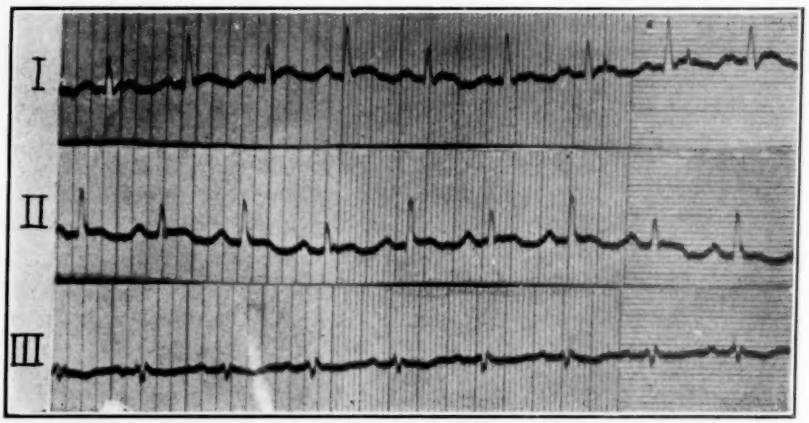


Fig. 1.—Electrical alternans in all three leads involving the QRS complexes. In Lead I the P-R interval in certain cycles is slightly prolonged, concordant with the QRS alternation. S-$T_1$ and S-$T_2$ are elevated and convex. Rate 120. Record taken April 20, 1936.

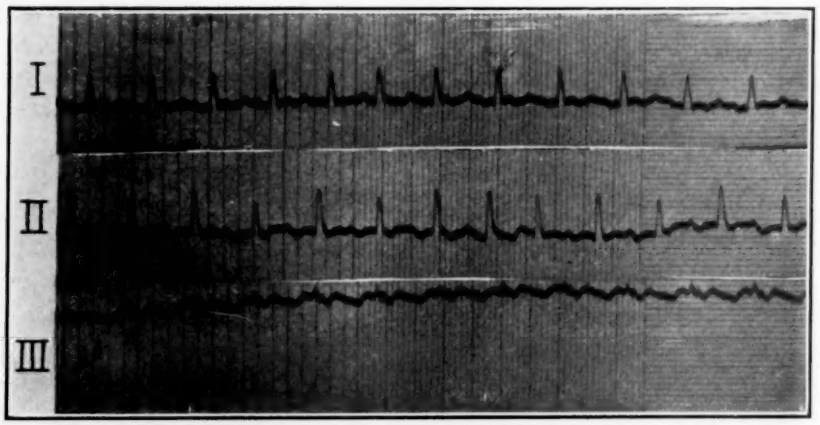


Fig. 2.—A 2:1 auricular flutter is present with a ventricular rate of 150. No electrical alternation in Lead I, but the QRS complexes are all low. In Lead II, there is transient electrical alternation, the high complexes being not quite as high, and the lower not quite as low as in the corresponding lead of Fig. 1. Record taken April 25, 1936.

with obliteration of Traube's space. The liver was not felt. There was no edema of back or extremities. There was no leucocytosis, the urine was not abnormal, and the Kahn test and routine blood chemistry showed no abnormalities.

Because of the distant heart sounds a bedside film was taken. It revealed a markedly dilated and hypertrophied heart, the enlargement being mostly in the region of the left ventricle, fluid in the left pleural cavity, and a slight amount of fluid in

the right pleural cavity. The configuration of the heart was such that neither the roentgenologist nor the consultant did as much as suspect fluid in the pericardium.

An electrocardiogram at this time (Fig. 1) showed upward convexity of the S-T segment in Leads I and II, and frank continuous electrical alternans of the QRS complexes in all leads. In Lead I the P-R interval of certain cycles was slightly prolonged concordant with the QRS alternation. Another electrocardiogram (Fig. 2) four days later showed a definite 2:1 flutter with a ventricular rate of 150 per minute, and absence of the alternans in Lead I, but the QRS complexes were all low. In Lead II there was a transient electrical alternans, the higher complexes being not quite as high and the lower complexes not quite as low as in the corresponding lead of Fig. 1.

The patient became rapidly worse and died nine days after admission. Necropsy by Dr. Israel Davidsohn revealed metastatic adenocarcinoma to the lungs, mediastinal glands, mediastinal pleura, and the pericardium. The pericardium contained 1,000 c.c. of a bloody fluid. The heart weighed 358 grams, the wall of the left ventricle measuring 14 mm. Grossly there was no evidence of infarction, fibrosis, or metastases. Both auricles were normal in size, and showed no evidence of metastases, special attention being paid to the region of the S-A node. The coronary arteries showed no abnormalities. The liver and kidneys showed a few metastatic nodules. The uterus, left adnexa, and right tube were absent and the right ovary was normal. The right breast presented an old scar.

Microscopic examination of the heart revealed slight increases in the interstitial connective tissue. In the subepicardial layers accumulations of lymphocytes and plasma cells were present. The pericardium was markedly thickened by loose, young granulation tissue which was infiltrated with a large accumulation of lymphocytes and plasma cells. In some areas large atypical epithelial cells were seen which had hyperchromatic nuclei and were similar to those seen in the tumor of the lung. Tissue examination for tuberculosis and guinea pig inoculation gave negative results. While the source of the metastatic carcinoma was not found, it was the opinion of the pathologist that it may have originated in the ovary or in the tumor of the breast that were removed some years previously in another hospital.

## COMMENT

The absence of the electrical alternans from Lead I of the second electrocardiogram (Fig. 2) does not necessarily indicate that the condition of the heart has improved, as it might appear at first thought. It is more likely, according to Hamburger and his associates,[4] that its disappearance has exactly the opposite significance. Alternans means that at a certain stage of heart weakness certain portions are unable to respond normally to every stimulus but fluctuate alternately between a better and poorer or even no response. As the myocardial weakness progresses the condition is changed and the heart may give a poor but constant response to every stimulus.[1, 4] This probably accounts for the constantly low QRS complexes in this lead. It is highly probable that the onset of the auricular flutter caused additional fatigue in an already embarrassed heart. On the other hand the reappearance of transient alternation in Lead II of this electrocardiogram may, paradoxically, indicate improvement of certain regions. However, that the heart is not

as strong as in the preflutter stage (Fig. 1) is indicated by the fact that the highest QRS complexes are not quite as high as those in the corresponding lead of the first electrocardiogram.

Since autopsy failed to elicit disease of the coronary arteries, extensive myocardial fibrosis, or metastatic lesions to the heart, the massive pericardial effusion is probably the cause of the electrical alternans in this case. It is not certain whether it is an isolated alternans or not, since the patient's pulse was not studied by an arteriogram. However, the patient's son, a well-trained physician who was in constant attendance gave the assurance of not having found a pulsus alternans by palpation or blood pressure determination.

That pericardial effusion may alter the voltage of the electrocardiogram is not unknown. Oppenheimer and Mann[15] and Gager[16] have described such changes. Scott, Feil, and Katz[17] produced among other electrocardiographic changes, lowered voltage in their experimental pericardial effusion. Harvey and Whitehill[18] found low voltage in eleven out of fifteen cases of pericardial effusion. They all attributed the change to the fluid which by its hydrostatic pressure caused anoxemia of the heart muscle. It was usual for the height of the deflections to increase, as the fluid was withdrawn, and the patient improved.

But that pericardial effusion may cause electrical alternans with or without pulsus alternans is not frankly recorded except for the remark by Harvey and Whitehill,[18] "Alternation in amplitude was occasionally observed, as were changes in the form of each second or third complex. These changes were present only in fairly large effusions."

The essential disturbance in electrical, as well as in mechanical alternans, is alternation in the physiological response of parts of the heart due to fatigue or malnourishment of certain fractions of the myocardium. Coronary disease has been found in almost all of the cases reported. The literature contains many references to the so-called coronary alternans. Lewis[19] was the first to demonstrate alternans of the heart following coronary occlusion. Condorelli[20] described electrical and pulsus alternans in man with disturbed coronary circulation, and also in dogs following coronary occlusion. Kisch[13] found that interference with the nutrition of the dog's heart through coronary closure may cause alternation, even when the pulse does not increase. The alternation promptly disappeared following the removal of the coronary ligature.

Now, it has been assumed during the last seven or eight years that pericardial effusion may interfere with the coronary circulation. This assumption was employed to explain the changes in the S-T segment and T-wave often seen in pericardial effusion, clinical and experimental.[16, 17, 21, 22] Katz and his associates[21] thought that the hydrostatic pressure within the pericardium caused a "herztamponade," and thus

compressed the vascular channels, leading to anoxemia. The removal of the fluid in their experimental animals restored the electrocardiogram to the normal.

Hence, it is easily conceivable that the anoxemia thus produced may, under certain circumstances, interfere with the intrinsic circulation of certain regions of the heart muscle and thus lead to alternation. The slight fibrosis and subepicardial infiltration in this case were in all probability noncontributory; the former being inconspicuous and the latter only localized. The effect of the hydrostatic pressure may vary widely, depending upon rapidity of filling, amount of fluid, and distensibility of the sac, according to Katz.[21] The electrical alternans then in this case with pericardial effusion was presumably caused by anoxemia and may be designated as the coronary type of Kisch, although the coronaries were structurally normal.

The auricular flutter developing a few days before death in the absence of metastasis to the auricles, is additional evidence of an existing anoxemia. That pericardial effusion may cause disturbance in cardiac rhythm and conduction is known. Gager[16] reported an instance of heart block that disappeared after the withdrawal of the fluid. Harvey and Whitehill[18] found two cases of auricular fibrillation, one ceased spontaneously, and the other immediately following the withdrawal of 800 c.c. of fluid. In the experiment of Katz[21] and his associates, arrhythmias were encountered which were abolished by removal of the fluid. Hence, the auricular flutter in this case is analogous to that seen in coronary disease—anoxemia being the essential cause in both instances.

## SUMMARY

A case of electrical alternans occurring in a patient with pericardial effusion is added to the literature.

Autopsy revealed carcinomatous pericarditis with 1,000 c.c. of bloody fluid. The coronary arteries were patent and not abnormal, and the myocardium showed only slight fibrosis.

It seems very likely that the hydrostatic pressure within the pericardial sac compressed the vascular channels and caused an anoxemia. The latter is conceivably the cause for the alternation, which may be designated as the coronary type of Kisch in spite of structurally normal coronary arteries. Changes in the S-T segment, frequently occurring in pericardial effusion, were also present.

Auricular flutter appeared a few days before death. In the absence of metastasis to the auricles, this arrhythmia is attributed to the anoxemia —resulting from "herztamponade."

Electrical alternans, like pulsus alternans, carries a grave prognostic significance.

## REFERENCES


1. White, P. D.: Heart Disease, New York, 1932, The Macmillan Company, pp. 246 & 595.
2. Chini,V.: Contribution a létude de l'alternance du Coeur, Arch. d. mal. du Coeur **21**: 90, 1928.
3. Missal, M.E., and Crain, R. B.: Alternation Phenomenon in the Electrocardiogram, AM. HEART J. **11**: 611, 1936.
4. Hamburger, W. W., Katz, L. N., and Saphir, O.: Electrical Alternans, J. A. M. A. **106**: 902, 1936.
5. Brody, Jacob G., and Rossman, Phillip L.: Electrical Alternans, J. A. M. A. **108**: 799, 1937.
6. Lewis, Thomas: Diseases of the Heart, New York, 1933, The Macmillan Company, p. 249.
7. Lewis, Thomas: Clinical Electrocardiography, ed. 5, 1931, Chicago Medical Book Company, p. 105.
8. Mines, G. R.: J. Physiol. **46**: 349, 1913.
9. Condorelli, Luigi: Arch. di pat. e clin. med. **8**: 428, 1929.
10. Galata, G.: Cuore e circolaz **12**: 178, 1928.
11. Pezzi, C.: Arch. d. mal. du Coeur **15**: 378, 1922.
12. Chini, V.: Cuore e circolaz **11**: 494, 1927.
13. Kisch, Bruno: Der Herzalternans, Leipzig, 1932, Theodor Steinkopff.
14. Katz, L. N.: Quoted by Brody and Rossman in reference 5.
15. Oppenheimer, B. S., and Mann, H.: An Electrocardiographic Sign in Pericardial Effusion, Proc. Soc. Exper. Biol. & Med. **20**: 431, 1923.
16. Gager, L. T.: The Conduction Changes Accompanying Pericardial Effusion, Arch. Int. Med. **33**: 499, 1924.
17. Scott, R. W., Feil, H., and Katz, L. N.: The Electrocardiogram in Pericardial Effusion (Clinical), AM. HEART J. **5**: 68, 1929.
18. Harvey, A. M., and Whitehill, M. R.: Tuberculous Pericarditis, Medicine **16**: 45, 1937.
19. Lewis, Thomas: Quart. J. Med. **4**: 141, 1910.
20. Condorelli, Luigi: Die Ernehrung des Herzens, Leipzig, 1932, Theodor Steinkopff.
21. Katz, L. N., Feil, H., and Scott, R. W.: The Electrocardiogram in Pericardial Effusion, AM. HEART J. **5**: 77, 1929.
22. Schwab, E. H., and Hermann, G.: Alteration in the Electrocardiogram in Diseases of the Pericardium, Arch. Int. Med. **55**: 917, 1935.

# Special Article

## STANDARDIZATION OF PRECORDIAL LEADS

JOINT RECOMMENDATIONS OF THE AMERICAN HEART ASSOCIATION AND THE CARDIAC SOCIETY OF GREAT BRITAIN AND IRELAND

In the last few years, electrocardiographic leads in which an electrode placed upon the precordium is paired with an electrode in contact with some part of the body distant from the heart have come into widespread use. The confusion which has resulted from the lack of uniformity and precision in the technique and nomenclature employed by different observers in connection with leads of this kind has led to an almost universal desire that a standard practice be established. To this end the American Heart Association and the Cardiac Society of Great Britain and Ireland have each appointed a committee to consider this matter and make recommendations. The two committees have conferred and have agreed jointly to make recommendations with reference to the routine use of a single precordial lead. It is understood that either committee may make additional reports with reference to multiple precordial leads and other matters not dealt with in the present report.

1. It is recommended that those who employ a single precordial lead place the precordial electrode upon the extreme outer border of the apex beat, as determined by palpation. If the apex beat cannot be located satisfactorily by palpation the electrode may be placed in the fifth intercostal space just outside the left border of cardiac dullness, or just outside the left midclavicular line if percussion of the heart is unsatisfactory. Where precordial leads are taken by a technical assistant, the position for the precordial electrode should be marked on the chest by the physician.

2. It is recommended that a single precordial lead in which the precordial electrode has the location specified in the preceding paragraph be known as Lead IV B when this electrode is paired with an electrode in the left interscapular region; Lead IV R when it is paired with an electrode on the right arm; Lead IV L when it is paired with an electrode on the left arm; Lead IV F when it is paired with an electrode on the left leg; and Lead IV T when it is paired with a central terminal connected through equal resistances of 5,000 or more ohms to electrodes on each of the three extremities mentioned.

*It is suggested that for all ordinary purposes Lead IV R or Lead IV F be employed. The latter lead should have the preference until it has been established that the former, which is somewhat more convenient, is equivalent to the latter for all practical purposes, or yields results of equal value.*

3. It is recommended that in taking the precordial leads specified the galvanometer connections be made in such a way that relative positivity of the apical electrode is represented in the finished curve by an upward deflection (a deflection above the isopotential level) and relative negativity of the apical electrode by a downward deflection.

It is urged that this convention be adhered to in the case of precordial leads other than those specified, and also in the case of all leads in which one electrode is placed much closer to the heart than the other. In other words, it shall be the standard convention in taking such leads to make the galvanometer connections in such a way that relative positivity of the electrode nearer the heart is represented by an upward deflection.

4. It is recommended that with the galvanometer connections made as described in the preceding paragraph, the deflections of precordial leads be designated by the symbols P, Q, R, S, and T, and that in the application of these symbols the same conventions be employed as in the case of the standard limb leads.

5. It is recommended that in taking precordial leads the electrocardiograph be so adjusted that a deflection of one centimeter in the finished record corresponds to a potential difference of one millivolt as in the case of the standard limb leads. Any reduction in sensitivity made necessary by very large deflections should be clearly indicated on the curve preferably by photographing the effect of introducing a potential difference of one millivolt into the galvanometer circuit.

6. It is recommended that the greatest dimension of the apical electrode employed in taking the leads specified in this report be 3 cm. or less. A circular electrode between 2 cm. and 3 cm. in diameter should ordinarily be employed.

7. It is recommended that the terms Lead IV (R, F, etc.); apical lead, apex-leg lead, etc., be used henceforth only in connection with the leads specified in this report.

*Signed*

ARLIE R. BARNES
HAROLD E. B. PARDEE
PAUL D. WHITE
FRANK N. WILSON
CHARLES C. WOLFERTH

Committee of the American Heart Association on the Standardization of Precordial Leads.

D. EVAN BEDFORD
JOHN COWAN
A. N. DRURY
I. G. W. HILL
JOHN PARKINSON
P. H. WOOD

Sub-Committee of the Cardiac Society of Great Britain and Ireland on the Standardization of Chest Leads.

# Department of Clinical Reports

## BRUCELLA MELITENSIS BACTEREMIA ASSOCIATED WITH VEGETATIVE ENDOCARDITIS*

DANIEL F. LEVY, M.D., NEW HAVEN, CONN., AND BENJAMIN SINGERMAN, M.D., BURLINGTON, VT.

THERE is an impressive rarity of references in the literature to cases of endocarditis due to *Brucella melitensis*. In 1928, Scott and Saphir[1] reported one case and found only five additional references to cases of this nature. Since that time other single cases have been reported by Gate and Ravault,[2] De La Chapelle,[3] Casanova and Ignazio,[4] Gounelle and Warter,[5] and Rennie and Young.[6] De La Chapelle, in commenting on his case,[3] states that, "A survey of the literature failed to discover any fatal cases with necropsy findings of subacute bacterial endocarditis due to *Br. melitensis A.* in this country." He is careful to point out that among the few cases which had been reported with autopsy findings up to the time of his report the vegetative endocarditis was implanted on an old deformed valve or superimposed upon chronic (rheumatic) endocarditis. In the few cases which have been reported since De La Chapelle's, a careful scrutiny of the findings seems to indicate that the presence of an old endocardial lesion is the rule. In the present case there was undoubtedly evidence of preceding chronic mitral involvement, probably rheumatic in origin.

### REPORT OF CASE

J. S., a white male, fifty-four years of age, who had been a moulder for the past thirty years, entered the Grace Hospital on March 26, 1936. He complained of fever and chills. The past history included a very short attack of "malaria" at the age of nineteen. He had had a frostbite seven years before admission, and a fracture of the right clavicle shortly thereafter. The parents were both dead. The causes of death were unknown. There was no history of tuberculous contact. The patient had been having chills and fever for seven weeks before admission to the hospital. Early in this illness there had been a chill every day. The chills now occurred every second or third day, lasting from five to thirty minutes. There was complaint of marked weakness and lassitude. A review of the cardiorespiratory system revealed that there had been considerable coughing, productive in nature. The patient raised four to eight ounces of sputum daily. It had never been blood-streaked but was thin and watery. This cough had been present for four weeks prior to admission. There was no hemoptysis or epistaxis. There had been hoarseness for three weeks. Dyspnea had been present on exertion for the past few years. There was no ankle edema, precordial pain, or palpitation. His gastrointestinal history revealed

*From the Medical Service, Grace Hospital, New Haven, Connecticut.

anorexia for the past three weeks, associated with constipation. Stools were apparently normal. His genitourinary history revealed nocturia three or four times each night for several years. No dysuria or hematuria.

*Examination.* On admission temperature was 102.4° F. (rectally); pulse, 100; respirations, 24; and blood pressure, 120/80. The patient was a slender, sallow male, lying comfortably in bed in no distress. There was evidence of considerable loss of weight. Pupils were equal, regular, and reacted to light and accommodation. Nose and ears were negative. The teeth were in poor condition. The tongue was dry and slightly coated. There was no cervical adenopathy or rigidity. There was marked retraction of the supraclavicular fossae. The cardiac impulse was noted lateral to the anterior axillary line. A systolic thrill was felt over the apical area. In this same region a very loud systolic murmur was audible. This was transmitted to the axilla. The same murmur was heard over the entire precordial area and over the base. There was regular rhythm. Breathing at both apices was somewhat bronchovesicular both anteriorly and posteriorly. Numerous moist râles were present at the left base and over the right apex. The liver was slightly enlarged and a tender edge was palpable just below the costal margin. No petechia or icterus was noted. There was moderate clubbing of the fingers. No abdominal tenderness. No edema of the extremities. No impairment of the motor or sensory functions of the extremities. Reflexes were normal. Tentative diagnosis on admission was rheumatic heart disease, pulmonary tuberculosis, or pneumoconiosis.

*Admission Laboratory Data.*—Red blood count was 3,600,000; hemoglobin, 57 per cent (Dare); white blood count, 14,400, 84 per cent polymorphonuclears, 15 per cent mononuclears, 1 per cent eosinophiles. Blood sugar was 120 mg. per 100 c.c., nonprotein-nitrogen, 30 mg. per 100 c.c. The urine was cloudy, amber, acid with specific gravity 1.012, albumin 4 plus. Numerous white blood cells were seen under the microscope. Some of these were in clumps. There were also numerous red blood cells. The sputum was watery. There were a few epithelial cells. No pus cells and no tubercle bacilli were found. (Examination included concentration tests of sputum.) The smears showed chiefly gram-positive cocci, some in clusters, and many fusiform bacilli and spirilla resembling Vincent's organisms.

*Clinical Course.*—An X-ray film of the chest revealed what was thought to be pulmonary tuberculosis involving the upper halves of both lungs. The heart was situated medially. It gave the impression of being moderately enlarged in all diameters, most markedly to the left. The question of silicosis was seriously debated because of the man's lengthy service as a moulder. The right lung especially showed a generalized fibrosis throughout. On the left side this was present but not so markedly below the fourth rib.

During the first two weeks of the patient's stay in the hospital, chills occurred. These lasted approximately fifteen minutes on each occasion. They were usually three or four days apart and left the patient exhausted. Frequently there was profuse sweating. A productive cough was noted. At times the coughing spells were very severe. On one occasion after coughing there was an expectoration of a large amount of rust-colored sputum and also some sputum streaked with fresh blood. Toward the last two weeks of his illness the patient had occasional epistaxes. Sometimes the bleeding was profuse. The mucous membranes were almost colorless. Transfusion did not seem materially to alter the progress of the disease. Prostration became more and more marked.

After the first week in April the sclerae assumed a subicteric tint. Later the skin color was *café au lait.* Toward the end of the disease, jaundice was marked. Also, after the first week in April a loud diastolic murmur was heard in the pulmonic area. Frequent extrasystoles were observed. The abdomen was spastic and tender throughout. It was slightly tympanitic. Anorexia was severe. The patient was examined

daily for the appearance of petechiae. About the middle of April a single questionable one appeared in each conjunctival sac. A day or two later, examination of the eyegrounds revealed a hemorrhagic area in the left fundus just below and to the right of the optic disc and about three-fourths the diameter of the disc. On that occasion a definite petechia was seen in each of the lower conjunctival sacs, the one on the left having a central pinpoint whitish area. There were also observed several petechiae on the abdomen and in the right axilla. Small ecchymotic areas were present in the right axillary region. A few days later new conjunctival petechiae appeared and then they became very numerous over the chest, abdomen, and back. The spleen was not palpated at any time. During the last ten days it was noted that the left pupil was larger than the right. The tongue protruded slightly to the left and there was moderate nuchal rigidity. The left knee jerk was hyperactive.

With the jaundice, the urine became very dark. Widal tests were negative for typhoid and paratyphoid A and B. No malarial parasites were seen. After the first week in April the blood culture was reported negative. On the tenth of April agglutination test for undulant fever was positive in dilutions of 1:50 and 1:150. No history of drinking goat's milk was obtained. Another blood culture made on April 13 was reported negative on April 16. However, these same flasks on April 23 showed a positive culture of *Brucella melitensis*. The agglutination test remained positive in a dilution of 1:150. Several blood counts during the hospitalization showed only a moderate increase over the original leucocytosis. The differential count remained approximately the same. Repeated examinations of the urine throughout the course showed very much the same picture as at entrance. The sputum remained repeatedly negative for acid-fast bacilli. Wassermann and Kahn tests were negative both on the blood and spinal fluid. The spinal fluid itself was clear. It was under normal pressure. The Pandy reaction was negative. Three mononuclears per cubic millimeter were found in it. A blood culture made on April 18 was reported on April 22 as showing approximately 5,000 colonies of *Brucella melitensis*, per cubic centimeter of blood. The temperature curve was of the septic variety, sometimes swinging up to nearly 105° F. and often subnormal. The pulse varied with the temperature. The respirations were never markedly accelerated.

About the middle of April the patient's blood pressure was only 80/50. With his rapid downhill course he became incontinent of urine and at times delirious. On April 22 his respirations were labored and the pulse was failing rapidly. On that day he died at about 10:50 A.M.

*Autopsy.*—The post-mortem examination was made by the pathologist, Dr. C. J. Bartlett. The summary of his findings are herewith given: The skin showed a moderate degree of jaundice. There were large numbers of minute petechiae over the front part of the chest and abdomen and also over the back.

On opening the abdominal cavity a small amount of clear liquid was present. The liver extended about one fingerbreadth below the costal margin. There were a few minute petechial hemorrhages in the parietal peritoneum.

There was no liquid in the pleural cavity. There was an old adhesion at each apex. The pericardial sac contained a little more clear liquid than the normal. On opening the heart with aseptic precautions, a vegetation could be seen attached to the mitral valve and a considerable portion of this was removed for culture and microscopic examination. Each side of the heart contained considerable thin liquid blood and soft moist chicken-fat clots. The mitral valve showed a friable vegetation somewhat over 1 cm. in diameter and one other area showed a small granular surface. In the wall of the left auricle there was one small slightly elevated vegetation. The mitral valve showed fibrous thickening in some areas, such as would result from chronic rheumatic valvular endocarditis. The valve was not much shortened and

presumably was competent. The larger vegetation referred to involved both the under and upper surfaces of the valve. This orifice measured 11 cm. The aortic, pulmonic, and tricuspid valves and orifices showed nothing of particular note. The heart weighed 410 grams chiefly due to hypertrophy of the left side. The cavities were somewhat dilated and the myocardium was flabby. The aorta was smooth.

Both lungs showed considerable black pigment. At each apex there was firm scar tissue with a large amount of black pigment. At the left apex this area of scar tissue was greater than at the right and measured about 5 or 6 cm. in diameter. This was the type of scarring which would result from an old tuberculous process though there was an excessive amount of pigmentation. No cavitation was found. Scattered throughout the remains of both lungs were numerous small black areas, some of which were considerably firmer than the surrounding lung tissue. This was interpreted as indicating some degree of silicosis but there was an abundance of functioning lung tissue. Bronchi, a little larger than normal, but no bronchiectatic cavities were recognized. The right lower lobe was congested and there was a little blood on the mucous membrane of the bronchus of this side which presumably came from this lobe.

The spleen weighed 620 grams. It showed numerous recent infarcts varying from 6 or 7 cm. in diameter down to much smaller ones. The pulp was reddish and soft but not so much so as in a typical septic spleen. The Malpighian bodies were readily recognizable.

The pancreas was negative.

The stomach showed several minute petechial hemorrhages in the mucous membrane particularly in the lower half and a very few were found along the course of the intestine.

The liver weighed 1,860 grams. It was in general smooth but on the convex surface of the left lobe, with proper illumination, there could be recognized very minute granules. These were not seen elsewhere. Aside from this the liver and gall bladder were not abnormal.

The suprarenal capsules showed nothing of note.

The kidneys had a combined weight of 415 grams. The capsules stripped readily leaving a smooth surface. The kidneys were pale yellow in color suggesting a mixture of a little bile staining with fatty degeneration. One kidney showed a recent infarct about one and one-half cm. in diameter and the other kidney showed a cyst of about the same size projecting above the cortical surface. A very few minute petechial spots were seen in the kidneys. The cortex was of good thickness. The bladder showed a few petechial spots.

The prostate showed nothing of note. The brain showed a little edema of the meninges. Nothing of note aside from a few minute petechial hemorrhages was recognized.

*The anatomical diagnosis* was subacute bacterial endocarditis of the mitral valve, chronic mitral endocarditis, myocardial degeneration, scars of old tuberculous lesions at apices of lungs. Some silicosis of lungs, acute infarcts in spleen and one kidney. Fatty degeneration of kidneys, minute petechial hemorrhages in skin and various organs. Slight amount of ascites. Bile staining of tissue in general.

Microscopically the myocardium showed nothing of particular note. The mitral valve showed some chronic thickening together with an acute inflammatory process. The exudate here was chiefly fibrin with comparatively few cells. In a section of the vegetation stained by the Gram-Weigert method there were present in the fibrin great numbers of minute granular structures, probably gram-negative bacilli. A smear made direct from the vegetation before fixation showed many small gram-negative almost coccoid bacilli.

Sections from the apices of the lungs showed dense fibrous tissue with much granular pigment. No tubercles or caseation were recognized. Neither here nor in any of the sections from other parts of the lungs was any active tuberculous process recognized. Sections from some parts of the lungs showed groups of pigment with a little increase in fibrous tissue around this but there was no considerable amount of fibrosis except in the sections from the apices. Sections from the right lower lobe showed a fair amount of blood and some desquamated epithelial cells in the air spaces. The small bronchi also appeared somewhat dilated.

The infarcted portion of the spleen showed the usual picture of acute infarct. Elsewhere there had been a hyperplasia of the spleen pulp with moderate increase in the connective tissue.

The liver and pancreas showed nothing of particular note.

The retroperitoneal lymph nodes showed considerable intercellular hyperplasia.

Microscopic examination of the intestines added nothing to the gross description.

A frozen section of the kidney stained for fat showed a great deal of this in the epithelial cells of the tubules in the cortex. It was in the form of fine droplets and indicated a marked parenchymatous degeneration. Some of the glomeruli showed more partial subdivision than normal and a few of them showed a cellular attachment to Bowman's capsule. Some also showed a few polymorphonuclear leucocytes inside of Bowman's capsule. Hyaline casts were present in some of the tubules. There were some areas of round cell infiltration between the tubules and the cortex. This appeared to be a diffuse inflammatory and degenerative process involving the tubules and to some extent the glomeruli.

The bone marrow of the femur was considerably more cellular than normal.

## COMMENT

Since the diagnosis of brucellosis is being made with greater and greater frequency, one should be alert to the possibility of bacterial endocarditis in this disease particularly when the patient has had a history of rheumatic or congenital heart disease. If blood cultures are done by the usual methods, one should not be deceived by the slow growth of the organisms.

## REFERENCES

1. Scott, R. W., and Saphir, O.: Brucella Melitensis (Abortus) Bacteremia Associated With Endocarditis, Am. J. M. Sc. **175**: 66, 1928.
2. Gate, J., and Ravault, P.: Mélitococcie. Endocardite infectieuse terminale, Lyon méd. **143**: 632, 1929.
3. De La Chapelle, Clarence E.: Vegetative Endocarditis Due to the Brucella Melitensis, Am. Heart J. **4**: 732, 1929.
4. Casanova, F., and Ignazio, C. D.: Vegetating Aortic Endocarditis Due to Brucella Melitensis, Minerva med. **2**: 209, 1933.
5. Gounelle, H., and Warter, J.: Ulcero-Vegetating Endocarditis During the Course of Melitococcemia, Bull. et mém. Soc. méd. d. hôp. de Paris **51**: 1197, 1935.
6. Rennie, J. K., and Young, C. J.: Malignant Endocarditis Due to Brucella Abortus, Brit. M. J. **1**: 412, 1936.

# PAROXYSMAL AURICULAR FIBRILLATION IN THE COURSE OF RIGHT HEART FAILURE DUE TO CHRONIC PULMONARY TUBERCULOSIS

## Case Report*

Milton B. Rosenblatt, M.D.
New York, N. Y.

IT HAS been well established that cardiac failure may be produced by a hypertension of the lesser circulation. In this type of failure the increased resistance in the pulmonary circulation results in hypertrophy and dilatation of the right side of the heart. While this condition may be due to a primary obliterating pulmonary arterial disease, it is more commonly due to chronic diseases of the lung.

One of the notable features of this form of cardiac insufficiency is the extreme infrequency of disturbances in cardiac rhythm. This point has been emphasized by White[1] and also by Smith,[2] who showed that the heart in pulmonary disease characteristically failed with normal rhythm. In a study of right heart failure previously reported[3] and in observation of these cases on the Tuberculosis Division for the past five years, this is the first instance of cardiac arrythmia that we have encountered due only to right ventricular failure.

S. G., a fifty-five-year-old baker, was admitted to the Montefiore Hospital on Sept. 20, 1936, with a history of pulmonary tuberculosis of twenty years' duration. With the exception of a brief period of hospitalization at the onset he had been able to work all the time and complained only of a moderate productive cough. In 1934, following an hemoptysis, there was an exacerbation of the pulmonary tuberculosis, and his condition became progressively worse up to the time of admission. In addition to his pulmonary symptoms he had experienced recurrent attacks of syncope since 1931. These seizures were brief, occasionally associated with convulsions, occurred about twice monthly, and recovery was spontaneous each time.

Physical examination showed the patient to be well developed, well nourished, and comfortable. There were no cardiac symptoms. The heart was not enlarged, there were no murmurs, and the rhythm was regular. The systolic blood pressure was 110 and the diastolic pressure was 60. The liver edge was palpable 2 cm. below the costal border but was not tender. There was no peripheral edema. Roentgen ray examination of the chest disclosed an extensive bilateral tuberculosis of the upper lobes with several large cavities. The cardiac outlines were within normal limits.

The important laboratory data are summarized as follows: Sputum, positive; Wassermann reaction, negative; urine, negative; blood chemistry, negative; red blood cells, 4,290,000; hemoglobin, 82 per cent; white blood cells, 12,500 with normal differential; sedimentation rate, 26 mm. in one hour; venous pressure, 4 cm. of water; electrocardiogram, normal except for low voltage.

*From the Tuberculosis Division of the Montefiore Hospital.

The clinical course in the hospital was characterized chiefly by recurrent large hemoptyses. However there was no remarkable change in his general condition until Nov. 3, 1936, when he suddenly became dyspneic, and examination revealed the pulse to be totally irregular. The cardiac rate at the apex was 140 per minute and the pulse rate was 116. There was no visible venous engorgement or peripheral edema. No electrocardiogram was taken at that time. The patient was rapidly digitalized and completely recovered within twenty-four hours. An electrocardiogram on the following day showed a normal rhythm. On November 14 the patient experienced a similar attack and a tracing taken during the seizure showed auricular fibrillation with a rapid ventricular rate (Fig. 1).

These episodes were repeated at approximately weekly intervals without any manifestations of congestive heart failure until Dec. 7, 1936, when, in the course of another paroxysmal attack, the dyspnea became progressively worse, and the patient became markedly cyanotic. The liver was enlarged to 4 cm. below the costal border, but there was no edema of the extremities. There was no response to therapy, and the patient died on Dec. 9, 1936.

On post-mortem examination the heart weighed 450 gm. There was no pericardial fluid. The right auricle and right ventricle were markedly dilated and hypertrophied, but the left auricle and ventricle were normal in size. The maximum thickness of the right ventricular wall was 10 mm. There was no valvular disease.

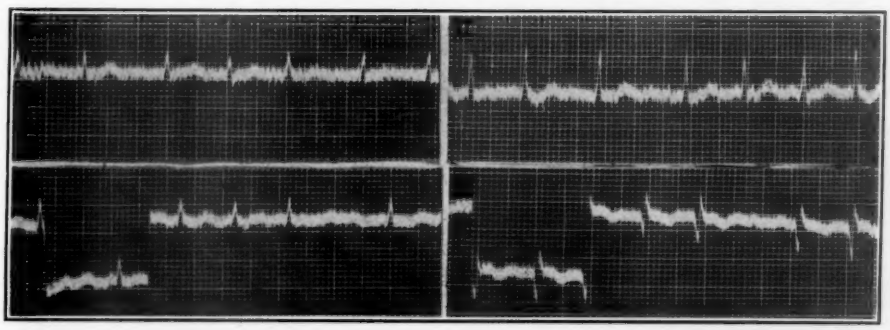

Fig. 1.

The coronary arteries showed slight sclerotic thickening but were patent throughout. Microscopic examination showed hypertrophy of the fibers of the right ventricle. Of interest in the examination of the lungs was the finding of extensive bronchiectasis which was indicative of the long duration of the pulmonary tuberculosis in this patient.

Auricular fibrillation, in itself, has been found on many occasions in patients on the tuberculosis wards. However, it has always been associated with hypertension, coronary artery disease, fibrinous pericarditis, or valvular disease. This is the first instance we have observed in which the only pathological condition found on autopsy was hypertrophy and dilatation of the right side of the heart.

## REFERENCES

1. White, Paul: Heart Disease, ed. 2, New York, 1937, The Macmillan Co., p. 739.
2. Smith, K. S.: The Heart in Pulmonary Disease, Post-Graduate M. J. 6: 43, 1930.
3. Nemet, G., and Rosenblatt, M. B.: Cardiac Failure Secondary to Chronic Pulmonary Tuberculosis, Am. Rev. Tuberc. 35: 713, 1937.

# REVERSIBLE BUNDLE-BRANCH BLOCK IN A CASE OF TOXIC GOITER

VICTOR A. DIGILIO, M.D.
PHILADELPHIA, PA.

BUNDLE-BRANCH block associated with hyperthyroidism seems to be a rare occurrence. The fortuitous encounter of such a case made follow-up electrocardiographic study necessary in order to determine whether reversion to the normal would occur as is frequently true of inverted T-waves in this disease.

The following case, seen on the cardiological service of Dr. J. B. Wolffe, is presented as an illustration of true reversible bundle-branch block because of a gradual change in the electrocardiographic picture following thyroidectomy rather than an abrupt reversion to a normal rhythm.

Mrs. M. R., aged twenty-nine years, was admitted on July 19, 1936, to the surgical service of Dr. Wayne W. Babcock at Temple University Hospital complaining of palpitation, nervousness, loss of weight, easy fatigability, prominence of the eyes, tremors, intolerance to warm weather but fondness for cold and ability to stand the cold with less covering than is required by the average individual. She stated that she was well until July, 1931, when she began to have the above symptoms. She was put to bed for six weeks by her doctor, who gave her iodine and four or five x-ray treatments to the neck. She felt better for a time, but there was no marked improvement. She became pregnant in 1932 and again in 1934, during which time practically all her symptoms disappeared. Five weeks prior to admission she experienced an exacerbation of the above symptoms and lost 15 pounds. Palpitation became frequent and severe and tremor of the hands so marked that on one occasion she dropped a sugar bowl. She began to have attacks of precordial pain without radiation. She was troubled with constipation, and her last menstrual period (one week prior to admission) lasted only two days whereas it previously lasted five days. There were no other symptoms.

Past medical history included measles, whooping cough, diphtheria, and scarlet fever in childhood. She had had no other illness. She has four children living and well. The family history is irrelevant.

Physical examination showed the following: White young-looking woman, mentally alert, of good color. There was no frank exophthalmos although her expression was somewhat "starey," and the palpebral fissures were somewhat widened. The thyroid was visibly enlarged. The peripheral vessels were soft. The pulse was rapid (120 per minute), equal in both wrists, and synchronous with the heart impulse. The apical impulse was diffused over a wide area and was tumultuous, causing the entire breast to rise and fall with systole and diastole. The cardiac outline was within normal limits to percussion. The heart sounds were loud. There was accentuation of the second pulmonic sound. No adventitious

sounds were heard. There was no evidence of cardiac failure. Laryngoscopic examination was negative. Fine digital tremors were noted. The blood pressure was 150/100. Impression: Toxic goiter.

*Laboratory Studies.*—Urine was yellow color, acid reaction, specific gravity 1.017, very slight trace albumin, negative sugar, no casts, no red blood cells and no white blood cells.

Blood count showed 70.4 per cent hemoglobin, 4,890,000 red blood cells, color index of 0.73, 5,350 white blood cells, 72 per cent polymorphoneutrophiles, 24 per cent lymphocytes, 3 per cent monocytes, and 1 per cent eosinophiles.

Basal metabolism on admission was plus 18 per cent.

Electrocardiographic examinations on July 20, 1936 (Fig. 1), showed left bundle-branch block (new nomenclature) and tachycardia.

Thyroidectomy was performed by Dr. Wayne W. Babcock on July 21.

On July 23 conduction disturbances although still present were greatly diminished.

On Sept. 4, 1936, there was complete absence of bundle-branch disturbance.

Fluoroscopic examination on July 20, 1936, showed that the heart was of normal size, shape, and position. There was no apparent enlargement of any of the

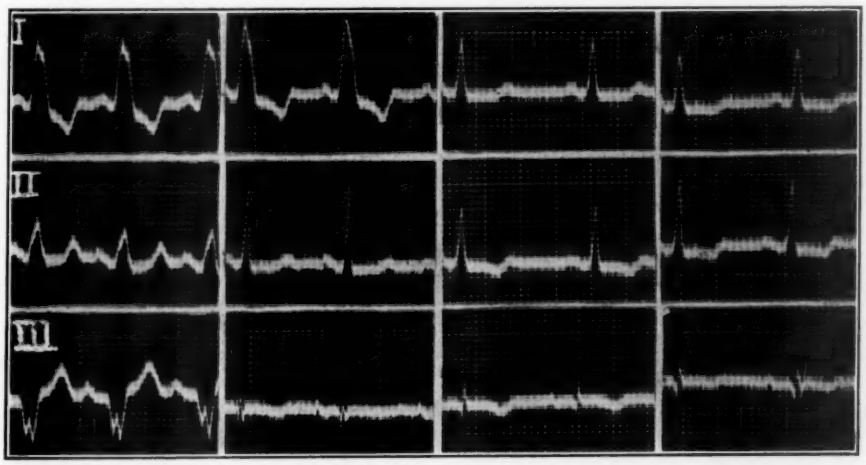


Fig. 1.—Reversible bundle-branch block in a case of toxic goiter.

chambers. The heart was markedly overactive. There was no abnormality of the aorta. The lungs were clear. The diaphragm was quite low.

On July 29 and Sept. 4, 1936, there was no change except that the heart was no longer overactive.

*Pathological Report.*—Gross description: Specimen consisted of several ragged pieces of pale, beefy thyroid tissue. The largest measured 6 × 2.5 × 1.8 cm.

Histological description: Microscopic sections showed the thyroid to be composed of large areas of more or less solid cellular tissue. Throughout this, tiny acini were seen. Here the picture suggested that of a fetal type of adenoma. In other areas the acini were somewhat larger and partly filled with colloid. The lining epithelium was of the cuboidal type. There were areas of hyalinized fibrosis. The thyroid stroma was cellular throughout with a few collections of small round cells. The diagnosis was involuting toxic goiter.

Sampson[1] quite recently saw a similar patient "who showed a recession from the bundle-branch block form after an acute cardiac episode at the termination of her thyrotoxicosis by thyroidectomy. The changes appeared rather gradually over a period of one week. . ."

## DISCUSSION

The cause of bundle-branch block in these cases is uncertain. Sampson feels that "... transient anoxemia of the heart muscle and conduction system" is responsible. Whatever the factor or factors involved, it can be said that bundle-branch block associated with hyperthyroidism may be reversible following appropriate therapy.

The significance of the last statement is apparent when one considers the possibility that a single electrocardiogram showing bundle-branch block may mislead the physician not only in the prognosis, despite a more hopeful outlook, but also in the diagnosis of a given case.

The above cases may be added to those reported by Sampson and Nagle,[2] Bishop and Bishop,[3] Wolff, Parkinson and White,[4] to modify our ideas regarding the prognostic significance of bundle-branch block.

## REFERENCES

1. Sampson, J. J.: Personal communication.
2. Sampson, J. J., Nagle, E.: The Prognosis of Bundle Branch Block and Other Intraventricular Conduction System Lesions, J. Am. M. Soc. **191**: 88, 1936.
3. Bishop, L. F., and Bishop, L. F., Jr.: Bundle Branch Block of Unusual Duration, Med. Rec. **145**: 16, 1937.
4. Wolff, L., Parkinson, J., and White, P. D.: Bundle-Branch Block With Short P-R Interval in Healthy Young People Prone to Paroxysmal Tachycardia. AM. HEART J. **5**: 685, 1930.

# HYPERPYREXIA AS A COMPLICATION OF RHEUMATIC FEVER

## REPORT OF A CASE*

JOHN A. BOONE, M.D.
CHARLESTON, S. C.

HYPERPYREXIA occurring during the course of acute rheumatic fever is a dangerous, but fortunately a rather rare complication of the disease. During the past fifty years there has been practically no mention of it in the literature, although the subject is treated at some length in most of the larger systems of medicine. Probably the best discussion, based on 110 cases collected from the older literature and his personal experience, was made by Sir William Church.[1]

It would seem to be exclusively an affection of adults, the youngest reported case being seventeen years of age. It is most common between the ages of twenty and thirty years and is rare after fifty. Males are affected more often than females in the ratio of approximately 3 to 2. The majority of instances occur during the first attack of rheumatic fever, the incidence diminishing in repeated attacks, and the mortality is greatest in those cases occurring in the first attack. There is no apparent tendency for an individual patient to have hyperpyrexia again in subsequent bouts of rheumatic fever.

In many the joint symptoms are relatively mild, and the patients are frequently said to have been in a depressed mental state prior to their onset. The appearance of hyperpyrexia usually is preceded by cerebral symptoms, though not uniformly, and most frequently comes in the second week of rheumatic symptoms. The joint manifestations are quickly clouded by excitability that may progress to mania or somnolence and stupor deepening to coma, and convulsions almost invariably supervene. Death from exhaustion or respiratory failure is the rule in untreated cases, and may occur in treated cases. Neither antipyretic drugs nor mild cooling measures have been effective. Only ice baths, promptly given and repeated as often as necessary, seem to have been of any marked value in saving life.

Post-mortem findings as described are very incomplete, since most of the reported cases occurred before histological examination of tissues was generally practiced. Descriptions of gross findings are remarkably negative, little besides congestion of the cerebral vessels and terminal pneumonia being found. The heart valves usually are conspicuously free from anatomical deformity.

*From the Medical and Pathological Services of the Peter Bent Brigham Hospital, Boston, Mass.

Because of the rarity of the condition, the paucity of post-mortem descriptions and the lack of recent literature on the subject, the following case is reported. It is the first case of hyperpyrexia complicating rheumatic fever to be admitted to the Peter Bent Brigham Hospital since it was opened in 1913.

## REPORT OF CASE

P. B. B. H. Med. No. 47100.—F. R. K., a forty-year-old native spinster, was admitted to the hospital at 2:30 P.M. on June 25, 1935 in a comatose condition. The family history revealed that the patient's father had died of a "heat stroke," but the history was otherwise irrelevant. As a child she had chicken pox, measles, mumps, and scarlet fever. Ten years before admission she was confined to bed for five months with rheumatic fever, but had no temperature higher than 103° F. at that time. She had frequent mild sore throats, but otherwise had seemed quite well all her life. For the past two years she had been considerably upset emotionally over conditions at her place of employment as a clerk and was given to frequent crying spells at home. Four weeks before entry she developed a nasopharyngitis with some swelling in the neck glands, which persisted several days. Two weeks before entry she noted some stiffness and soreness in various joints, and ten days before entry went to bed with more severe joint pains which were relieved by salicylates administered by her private physician. During the week before entry she began to have periods of irrationality at night, and three days before had a moderate nosebleed. Her temperature tended to rise during the night, but as far as known did not exceed 102° F. The day before admission she began to have a few mild twitching movements of various parts of the body and that night was completely irrational. The morning before admission she seemed stuporous and her temperature was found to be 105° F. She was then sent into the hospital.

Physical examination showed a well-developed and well-nourished middle-aged woman lying limply in bed, comatose, breathing stertorously in infrequent gasps. The rectal temperature was 109° F. (this was the upper limit of the thermometer scale). The pulse was small and thready, the rate 162 per minute. The respirations were not Cheyne-Stokes in character. The blood pressure was not obtainable. The skin was cold and clammy, the face and extremities cyanotic. Scattered over the thorax and abdomen were many tiny serum-filled blebs imparting a rough feel to the skin. Scattered infrequently over the whole body, more especially over the lower legs, were a few petechial hemorrhages. The eyes, including pupillary reflexes and ophthalmoscopic examination, were normal. The breath was foul, the lips and mucous membranes dry and cyanotic. The heart was of normal size, the sounds of poor quality, rapid and regular without murmurs. The lungs showed a few scattered râles and tracheal rhonchi. The abdomen was normal to palpation. No peripheral or tendon reflexes could be obtained.

Laboratory studies showed the blood Wassermann and Hinton reactions to be negative. The urine was clear, with specific gravity 1.011, and showed a very slight trace of albumin. The sediment contained rare red blood cells and a moderate number of coarsely granular casts. The blood showed hemoglobin 70 per cent (Sahli), red cell count 3.8 million, white cell count 27,000 with 75 per cent polymorphonuclears, 13 per cent small lymphocytes, 7 per cent large lymphocytes, and 5 per cent myelocytes. A stained blood smear was otherwise normal. A blood culture was negative. The blood urea nitrogen was 42 mg. per 100 c.c. A lumbar puncture shortly after admission showed normal pressure, Queckenstedt, chemistry, and Wassermann reaction.

Caffeine sodiobenzoate was given subcutaneously and an attempt was made to lower the extremely high temperature by wrapping the patient in a wet sheet and playing an electric fan over it. Under this regime the temperature slowly fell until after two hours it had reached 106° F. At about this time there began small twitchings of the lips and face and gradually the remainder of the body muscles became involved in the twitchings. The temperature continued to fall and by midnight had reached 103° F. The muscular twitching continued to spread and to increase in severity, no effect being had by carbon dioxide inhalations, calcium gluconate intravenously, or sodium phenobarbital subcutaneously. During the last five hours of her life the patient was in a continuous clonic convulsive state. She gradually became exhausted and died fourteen hours after admission to the hospital.

## POST-MORTEM FINDINGS

*Gross.*—The abdominal organs were normal with the exception of two small uterine fibroids and a small ovarian cyst. The heart weighed 280 grams. There were a few petechial hemorrhages scattered over the visceral pericardium but no evidence of pericarditis. In each auricle were small ante-mortem thrombi. The heart valves were entirely normal in appearance. The endocardium showed numerous tiny, slightly raised, white points near the attachments of the tricuspid valves, and three small petechial hemorrhages in the septal portion of the left ventricle. The lungs were normal aside from one small area of atelectasis and a few scattered petechial hemorrhages on the visceral pleura. The brain showed mild diffuse cerebral edema, venous congestion, and a distinct pressure cone at the base, involving cerebellum, pons, and medulla. There was a small meningioma, 4 mm. by 6 mm., over the right frontal lobe. The subarachnoid fluid was clear, showed no organisms or increased cells, and no exudate was seen. Close examination of sections, especially in the region of the basal ganglia, showed nothing abnormal. The superior longitudinal sinus and several of the cerebral veins showed ante-mortem thrombi.

*Microscopic.*—The heart showed a most striking active rheumatic involvement of myocardium, epicardium, and endocardium, including the mitral and tricuspid valves, as exemplified by Aschoff bodies in large number and in all stages of development. In one of the larger coronary arteries there was a lesion in the intima and media which was interpreted as being of an acute rheumatic type, and numerous vessels contained recent thrombi. One section showed a nerve trunk coursing in the epicardial fat, and involving this nerve was a typical Aschoff body. There was some very slight scarring through the myocardium, interpreted as being probably the healed lesions of the previous attack of rheumatic fever. In the sections from the aortic sinus and the arch of the aorta there was prominent thickening of the adventitia, swelling and fragmentation of the collagen, and numerous strands of fibrinoid material. Into this matrix there was prominent infiltration with monocytes, multinucleated cells, lymphocytes, and small numbers of polymorphonuclear leucocytes. About the numerous small vessels small groups of Aschoff cells were seen. Similar changes were seen in the pulmonary and renal arteries. The remaining viscera showed little of importance aside from frequent fibrinous thrombi in small vessels. Sections of the brain, including cerebral cortex, basal ganglia, pons, medulla, and cerebellum, showed nothing aside from engorgement of vessels with occasional thrombi and slight to moderate edema. Fiber tracts and cells were well preserved. The pituitary showed an area of hemorrhage in the pars intermedia about the size of one low power field. It extended laterally into the interstices of the dense collagen of the dura and slightly into the pars anterior and pars nervosa, but principally it infiltrated the fibrous tissue in the pars intermedia and lay about the cuboid-line spaces. It con-

sisted principally of red cells, but there were masses of free pigment and several instances of phagocytosis of pigment. In one region there were a few small strands of fibrin among the cells.

## COMMENT

The mechanism of the production of hyperpyrexia in rheumatic fever is quite obscure. The only lesion found in this case that by any chance might be conceived to have been of causative effect was the pituitary hemorrhage, but there is no evidence that such a lesion can cause hyperpyrexia. Granted that such an excessively high temperature is of "cerebral origin," there is a possibility that one of the widespread small-vessel thromboses might have involved the hypothetical "heat center" of the brain.

The case reported was probably beyond any therapeutic measures when first seen in the hospital. It would seem, however, that since hyperpyrexia tends to appear rather late in the rheumatic attack, and nearly always signals its imminence by symptoms of cerebral disturbance, it could be watched for by taking frequent temperature readings and controlled in its early stages by simple physical measures.

## REFERENCE

1. Church, Sir William: Allbutt and Rolleston, System of Medicine, London, 1912, The Macmillan Company, Vol. 2, p. 625.

# The American Heart Journal

VOL. 15 JANUARY, 1938 No. 1



EDITOR-IN-CHIEF
FRED M. SMITH
IOWA CITY

ASSOCIATE EDITORS
HUGH MCCULLOCH, ST. LOUIS
IRVING S. WRIGHT, NEW YORK CITY
HORACE M. KORNS, IOWA CITY

EDITORIAL BOARD

EDGAR V. ALLEN, Rochester, Minn.
CLAUDE S. BECK, Cleveland
HARRY GOLDBLATT, Cleveland
GEORGE HERRMANN, Galveston
WILLIAM J. KERR, San Francisco
ROBERT L. LEVY, New York City
H. M. MARVIN, New Haven
JONATHAN C. MEAKINS, Montreal
ROY W. SCOTT, Cleveland
ISAAC STARR, Philadelphia
J. MURRAY STEELE, New York City
PAUL D. WHITE, Boston
FRANK N. WILSON, Ann Arbor
CHARLES C. WOLFERTH, Philadelphia



**Official Organ of the American Heart Association**



Contents of this Journal Copyright, 1938, by The C. V. Mosby Company
All Rights Reserved



Application made at the Post Office at St. Louis, Mo., as Second-Class Matter


## Editorial

The AMERICAN HEART JOURNAL, under the editorship of Dr. Lewis A. Conner, has attained a position of distinction. Great honor is due Dr. Conner for the service that he has rendered in the development of a journal that is having a significant influence on the progress and practice in this field of medicine. It is hoped that the high scientific and literary standards set by him may be maintained.

The new Editor-in-Chief is aware of his responsibilities, and with the help of the Associate Editors and the Editorial Board, will strive to promote the further development of the AMERICAN HEART JOURNAL.

*Fred M. Smith.*

# Department of Reviews and Abstracts

## Selected Abstracts

**Hess, W. R.: Central Regulation of Circulation and Respiration. II. International Medical Week, Lucerne, 1936.** Abstracted from Ztschr. f. Kreislaufforsch. 29: 370, 1937.

The central nervous system coordinates the state of the respiratory and circulatory systems according to the needs of the moment. There is a unity between the nervous system and the physiologic state of the organs affected. The part of the nervous system involved in stimulating respiration and circulation is the sympathetic nerves, and that for conserving their activities is the parasympathetic nerves. The centers are in the medulla and hypothalmus.

L. N. K.

**Dressler, Wilhelm: Pulsations of the Wall of the Chest: I. General Consideration.** Arch. Int. Med. 60: 225, 1937.

Examination by means of simple inspection and palpation is almost always sufficient to demonstrate diagnostically important pulsatory findings. The graphic registration serves merely to control the clinical findings; it should be carried out with the fixed receptor.

Pulsatory movements of the thoracic wall are essentially caused by the effect of change in shape and diminution in volume of the heart. Hypertrophy and dilatation of the right chamber in association with the dilatation of the left auricle, as encountered in cases of lesions of the mitral valve of a severe degree, lead to a forceful systolic propulsion of the precordial area near the sternum.

Systolic depressions of the thoracic wall are due to the centripetally directed movement of the cardiac systole, which exerts an aspiratory effect on the thoracic wall in two ways: (1) directly, when the heart is in contact with the thoracic wall, and (2) indirectly, owing to the fall in intrathoracic pressure caused by systole. The effect of these aspiratory forces on the thoracic wall is equalized under normal conditions mainly by two factors: (1) the oppositely directed propulsive force due to the systolic change in shape of the heart and (2) the expansion of the lungs.

Pathologic depressions of the thoracic wall during systole are due to (1) marked increase of the systolic aspiratory effect (reduction of ventricular volume during the systolic efflux), (2) inhibition of the systolic change in shape of the heart, and (3) inhibition of the expansion of the lungs.

An increase of the stroke volume much more commonly causes systolic depression of the thoracic wall than do adhesions of the pericardium.

The liver may transmit its pulsatory movements to the adjacent thoracic wall. Normally the systolic efflux of venous blood from the liver often causes a depression of the portions of the thoracic wall in front of it. The systolic depression is often particularly marked in the presence of aortic regurgitation; this is due to the

increase in stroke volume and the increased aspiratory effect. Tricuspid regurgitation as a rule causes a forceful systolic propulsion of the hepatic area. The systolic impulse of the blood regurgitating into the large right lobe of the liver transmits to the whole chest a frontal movement directed from left to right. A presystolic propulsion of the thoracic wall over the hepatic area is often noted in congestive failure of the right side of the heart but particularly in the presence of tricuspid stenosis, provided the auricle is still capable of contraction.

In addition to primary pulsatory phenomena, which occur directly at the place of the pulsatory impact, secondary pulsations or associated pulsatory movements are observed. They should be looked on as distinct effects of the primary pulsatory forces. Pulsatory movements of the whole chest in a frontal direction are caused by a compensatory effect of both types of pulsations; this is observed when there is marked hypertrophy of the left ventricle, tricuspid regurgitation, or mitral regurgitation, associated with aneurysmal dilatation of the left auricle to the right.

AUTHOR.

**Hallock, Phillip, and Benson, Ikel C.: Studies on the Elastic Properties of Human Isolated Aorta.** J. Clin. Investigation **16**: 595, 1937.

A method for experimentally obtaining the volume-elasticity coefficients of isolated aortas has been described.

The mean volume-elasticity curves demonstrate that arterial rigidity increases, (a) progressively with age and (b) with increasing diastolic pressure.

The aorta of old age assumes the rôle of a capacity chamber or reservoir and by virtue of this readjustment it becomes adapted to the reception of the cardiac output without imposing an undue strain on the heart, a condition which would otherwise result if the disappearance of elastic tissue occurred without a concomitant increase in the diameter and length of the aorta.

If the pulse wave velocities are calculated from mean volume-elasticity curves and compared with the mean pulse wave velocities obtained in living man at corresponding ages, it is found that the mean values obtained on the isolated aorta are less than those obtained in vivo by about 6 per cent. In the study of isolated aortas, the velocity values are slightly low due largely to the factor of elastic "after-action."

Due to the satisfactory agreement of the pulse wave velocities found in vivo and in the isolated aortas it is possible to evaluate the condition of the aorta in living man by comparison with an isolated aorta having approximately the same pulse wave velocity.

AUTHOR.

**Levine, Samuel A.: Presence of Digitalis in Body Fluids of Digitalized Patients.** Arch. Int. Med. **60**: 240, 1937.

A patient with cardiac disease who is digitalized and who yet shows peripheral edema or free fluid in the body cavities occasionally has symptoms of headache, nausea, vomiting, giddiness, and lassitude after diuresis induced with salyrgan or mercurin or with theophylline. These symptoms could be due to digitalis intoxication when the body fluids are excreted through the kidneys by way of the blood stream, if that body fluid contained digitalis substances.

On the basis of the chemical method of Schmidt, modified in terms of the physical properties of digitoxin, edema fluid from the pleurae, peritoneum, and leg was treated and concentrated, with the recovery of a gray white precipitate. This

precipitate, suspended in Clark's solution, was placed in a Straub preparation of the frog heart to be tested for digitalis, and the results were recorded on a kymogram. These curves were compared with curves for known digitalis.

A total of twenty-nine specimens of fluid from twenty-four patients was examined. Eighteen fluids were from known digitalized patients. Thirteen of these gave positive evidence of digitalis by the biologic method. The results were questionable in four cases and negative in one case. Two specimens from patients with questionable digitalization gave doubtful results. Nine specimens of fluids from patients with tuberculosis, neoplasm, or cirrhosis of the liver, none of whom had been given digitalis, were used as controls. None of these showed any digitalis effect.

Although no exact quantitative determinations were carried out for the thirteen fluids showing curves indicative of a digitalis effect, we believe the amount recovered was significant and sufficient to cause clinical symptoms in patients under the conditions discussed.

The Knudson-Dresbach reaction for the quantitative determination of digitalis glucosides was unsatisfactory in our experience. The qualitative Keller-Kiliani test for desoxycarbohydrate, though not specific and not highly sensitive, gave positive reactions for five of eleven specimens of fluid showing the digitalis effect by the biologic method.

It is believed that active digitalis substances are present in the body fluids of digitalized patients and that they can be recovered. Further studies are necessary, however, to confirm or to discredit the idea that these substances may give rise to symptoms of digitalis intoxication following diuresis.

AUTHOR.

**Condorelli, L.: The Pneumomediastinum in Cardiological Diagnosis.** Cardiologia 1: 26, 1937.

The author describes his anatomical investigations and presents evidence in favor of a "septum fibrosum" between the anterior and posterior pneumomediastinum. The significance of pneumomediastinum in cardiological diagnosis is discussed, with special reference to the condition of adherent pericarditis.

AUTHOR.

**Mahaim, I., and Benatt, A.: Studies on the Superior Connections of the Left Branch of the Bundle of His-Tawara With the Interventricular Septum.** Cardiologia 1: 61, 1937.

In men there are branches from the left bundle of His which supply the muscle of the interventricular septum. These arise high up near the bifurcation of the main bundle.

These branches are very small and can only be demonstrated by most careful and systematic investigation. In normal conditions they are of very little importance but they may account for some anomalous results observed in clinical cases of branch-bundle lesion.

AUTHOR.

**Blumberger, K.: The Differentiation of Two Types of Sino-Auricular Block.** Deutsche med. Wchnschr. 62: 1377, 1936.

Partial S-A block can be differentiated in much the same way as A-V block. The one type shows the equivalent of the Wenckebach period; the second does not.

L. N. K.

**Geraudel, E.: A Case of Auriculo-Ventricular Dissociation With Tachycardia.** Cardiologia 1: 9, 1937.

The author describes a case of sinus tachycardia with partial block which he has observed for fourteen years. The frequency varied from 120 to 200 per minute. Occasionally, the records showed signs of heart block. The relations of the observed changes to auricular flutter are discussed.

AUTHOR.

**Kisch, Bruno: Intermediate Waves in the Electrocardiogram.** Cardiologia 1: 17, 1937.

Attention is drawn to the occasional occurrence of certain typical positive waves in the electrocardiogram which have not been previously considered. These are the following:

There are two extra waves between R and Q, one immediately following P and the other immediately preceding Q. If Q is absent the latter precedes R. There is another wave between S and T, or if S is absent between R and T.

AUTHOR.

**Sigler, Louis H., Stein, Isidore, and Nash, Philip I.: Electrocardiographic Changes Occurring at Death.** Am. J. M. Sc. **194**: 356, 1937.

Electrocardiographic studies were made on 20 cases before, during, and after clinical death. The changes noted were: sinus tachycardia, followed by sinus bradycardia and sinoauricular standstill; development of ectopic foci of irritability, resulting in nodal rhythm, single and multifocal ventricular premature contractions and ventricular paroxysmal tachycardia; appearance and disappearance of auricular activity; auriculoventricular block in various degrees; ventricular fibrillation; marked changes in the initial and terminal ventricular complexes; intraventricular conduction disturbances in various degrees up to bundle-branch block. In many cases the electrocardiographic manifestations were noted as long as one hour after clinical death.

The factors responsible for these electrocardiographic changes appear to be disturbances in the vagosympathetic control of the heart, anoxemia, toxemia, and local nutritional and ionic disturbances in the heart. That anatomic disease of the heart itself is not responsible for the ultimate manifestations is evidenced from the fact that these changes occurred in the normal as well as in the diseased hearts. The sinus slowing and standstill, as well as the various grades of auriculoventricular block, appear to be mainly of vagal origin. Intraventricular disturbances are dependent on the other factors. The latter disturbances depict changes in the distribution of the excitation waves and the order of excitation and retraction as well as transient focal blocking and localized partial or total refractoriness.

AUTHOR.

**Weiss, Soma, and Wilkins, Robert W.: Myocardial Abscess With Perforation of the Heart.** Am. J. M. Sc. **194**: 199, 1937.

The two cases of solitary myocardial abscess with perforation of the heart are described. In the first case the abscess, caused by *S. aureus,* ruptured into the right ventricle as well as into the pericardial sac. In the second case the abscess, caused by pneumococcus, was localized mainly in the fat tissue at the junction of the auricle and ventricle and was formed as a direct extension of a small mural pneumococcus

vegetation. This abscess ruptured into the pericardial sac. In both cases the clinical course did not suggest sepsis and the unexpected cardiac perforation resulted in a fatal circulatory collapse.

While abscess of the myocardium in cases of sepsis is not an unusual occurrence, perforation of the heart by abscess is rare. Seven such instances, collected from the literature, are cited. As judged from the nine cases now available, myocardial abscesses are silent until their rupture causes sudden low thoracic pain, followed by circulatory collapse. In two of the nine cases a diastolic murmur was present.

AUTHOR.

**Narat, J. K.: A New Electrical Stethoscope.** Ztschr. f. Kreislaufforsch. **29**: 313, 1937.

A contact Rochelle crystal microphone was used with a button attached to be placed against the chest. The current is amplified by a 4-stage radio amplifier and through a tone filter. This method is also used for pulse records. Records were made on film.

L. N. K.

**Molz, B.: A Method of Obtaining Unipolar Leads in the Electrocardiogram.** Ztschr. f. Kreislaufforsch. **29**: 361, 1937.

Previous methods of obtaining unipolar electrocardiograms are not free of theoretical objections. A new method is described. A person is placed up to his neck in a wooden bath containing warm conducting solution and an extensive wire mesh. The wire mesh gives the potential of the entire body and this shows practically no change during the heart beat. This mesh is used as the indifferent electrode.

L. N. K.